Proceedings of the

American Philosophical

Society

Held at Philadelphia for Promoting Useful Knowledge

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Contrasts in Scientific Style

Emil Fischer and Franz Hofmeister: Their Research Groups and Their Theory of Protein Structure*

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Introduction

Since the middle of the nineteenth century, laboratory experimentation in the chemical and medical sciences has become increasingly the collective activity of research groups. In chemistry, the pattern set in the 1840s by Justus von Liebig in Giessen—the association of students, assistants, guests and technicians with a leader—developed rapidly in Germany, and was fostered by the growth of chemical industry.[1] After 1870, relatively large research groups became a lasting feature of German university institutes of chemistry. Similarly, the rise of scientific medicine in German-speaking countries, and the wider distribution of health care, promoted the establishment of research groups in university institutes of pathology, physiology, pharmacology, and bacteriology, as well as in some clinical departments of medical schools. The names Rudolph Virchow (Berlin), Carl Ludwig (Leipzig), and Oswald Schmiedeberg (Strassburg) are prominent in the history of this development.[2] These chemical and medical research groups, and the men who led them, attracted many foreign students, and exerted

considerable influence on the organization of scientific research abroad. Moreover, the success of the German research groups stimulated the creation, between 1885 and 1910, of separate research establishments, notably the Pasteur, Lister, Rockefeller, and Kaiser-Wilhelm institutes, where the members of research groups were free of university obligations.[3]

The styles of leadership varied widely. At one extreme, the leader was a quasi-military director of the work of subordinates, and at the other, a senior counselor in the independent efforts of his junior scientific associates. Apart from the personality of the group leader, and the number and caliber of his students and assistants, other factors affected the balance between dictatorship and liberality. Perhaps the most important of these was the institutional status of the discipline, but more general social factors in different nations or institutions, and at different times, inclined a leader to adjust his attitude toward the junior members of his group in order to promote its productivity.[4]

The award of credit for the research achievements of a closely-directed group has usually gone to the leader, as it was considered that he (or she) formulated the plan of attack that proved to be successful. Although some of the junior associates may have made original contributions to the success of the

group effort, they were expected to gain satisfaction from the reflected fame of their leader, and to hope that he would make their contributions known, especially to prospective employers. On the other hand, if the group leader acted principally as senior counselor to his junior associates, and his name did not appear among the authors of their research papers, his contributions to any success they may have achieved usually did not receive recognition, even if he may have suggested the research problem, given advice about the conduct of the work, and helped to write up the results for publication. His place in the historical record has been based largely on his personal research, usually performed at the beginning of his professional career.[5]

These general features of the scientific life have long been appreciated by the participants, and find reflection in their autobiographical writings and in accounts of their careers by others. With a few notable exceptions, however, historians of science have not studied sufficiently closely the role of research groups in the development of the chemical and medical sciences. The new insights gained from contributions such as those of Morrell and Geison amply demonstrate the importance of this approach.[6] Much attention has been given to the work and thought of individuals in an effort to discern the sources of their success as creative scientists. This is an important historical enterprise, especially when the individual was the chief experimenter in a small research group, or worked alone. But do the same criteria apply to leaders of large research groups? Moreover, does not the exclusive focus on the research achievements attributed to the group leader neglect the fact that research groups produce not only new scientific knowledge, but also the next generation of scientists?

One of the purposes of this essay is to ask whether there is a connection between the success of a research group in scientific discovery and invention (as measured, for example, by the award of a Nobel Prize to its leader) and the role of that group in turning out future leaders in their discipline. In an article published in 1967, Hans Krebs, whose research achievements place him among the great biochemists of this century, presented a diagram to suggest that a chemist or biochemist has had a better chance of winning a Nobel Prize if he had worked in the laboratory of another winner.[7] There is much in Krebs's article that I admire, but I believe that his genealogical approach casts only dim, and perhaps misleading, light on the relation between the fame of a group leader and the later distinction of his scientific progeny. Some of the questions that are left unanswered by such selective genealogy are: How large was the group of which the later Nobelist had been a junior member? What did he do as a member of the group, and what connection did that work or his leader's scientific writings have with his subsequent research? As for the non-winners, how many later gained distinction in chemical or medical research, and can their contributions be linked to their prior association with the group leader? What happened to the others, especially those whose names disappeared from the scientific literature after they left the group?

In this essay I will consider some of these questions as they relate to two research groups active at the turn of the century—one led by Emil Fischer (1852–1919) in organic chemistry at the University of Berlin and the other, in physiological chemistry, led by Franz Hofmeister (1850–1922) at the University of Strassburg, a German city between 1871 and 1918. Although an appreciation of these two men will require an account of their earlier careers, I will focus on the period from about 1899 to about 1914, when Fischer and Hofmeister were leaders of the most important German research cen-

ters in their areas of science, and when both men were interested in the same scientific problem, albeit from different points of view.

A MEETING IN KARLSBAD

The scientific link between Fischer and Hofmeister lies in the problem of protein structure. By an accident of history, that link was forged on a single day, 22 September 1902, at the 74th annual meeting of the prestigious *Gesellschaft der deutscher Naturforscher und Ärzte* in Karlsbad.[8] The first of the plenary lectures was presented during the morning by Hofmeister, under the title *Ueber den Bau des Eiweissmoleküls*. On the afternoon of the same day, in the third paper at the first session of the Section of Chemistry, Fischer gave a report *Über die Hydrolyse der Proteinstoffe*. In both talks, the theory was advanced that in proteins the constituent amino acids are joined to each other by the condensation of the amino group (NH_2) of one amino acid with the carboxyl group (COOH) of another amino acid to form amide (CO$-$NH) bonds in a linear structure to which Fischer gave the name *peptide*. In subsequent accounts of the history of protein chemistry, these two lectures mark the appearance of the so-called Fischer–Hofmeister peptide theory of protein structure.[9]

The organizers of the Karlsbad meeting clearly attached importance to Hofmeister's lecture, and the complete text appeared shortly afterward in successive issues of the widely-circulated weekly *Naturwissenschaftliche Rundschau*.[10] A major part of the lecture dealt with the mode of linkage of amino acids in proteins. After considering various earlier proposals, Hofmeister presented several arguments in favor of the view that the amino acids are joined largely by amide bonds. He attached special significance to the biuret reaction—the purple color given with alkaline copper sulfate by proteins and by intermediate products of their enzymatic digestion (the so-called albumoses and peptones).[11]

Among the synthetic materials (aside from biuret, $NH_2CONHCONH_2$) that give this color test, Hofmeister cited the products obtained by Curtius during the early 1880s either by the self-condensation of glycine ethyl ester ($NH_2CH_2CO-OC_2H_5$) to form a *biuret-base* or by the reaction of benzoyl chloride with silver glycinate. In the latter process, one of the isolated products was hippuryl-glycine ($C_6H_5CO-NHCH_2CO-NHCH_2COOH$), which in retrospect may be considered to represent the first synthetic peptide derivative.[12] In favor of his theory, Hofmeister also offered evidence from physiological studies on the enzymatic cleavage of proteins and of hippuric acid ($C_6H_5CO-NHCH_2COOH$). It should also be noted that he took occasion to hail the entry of Fischer into the protein field.

The paper read by Fischer on the afternoon of 22 September was not published in full, but an abstract prepared by him was printed a few weeks later in the *Chemiker-Zeitung*.[13] In this *Autoreferat* Fischer summarized his recent results on the isolation of amino acids and peptides from protein hydrolysates, and proposed that "in analogy to the known designation of carbohydrates as disaccharides, trisaccharides, etc., the substances of the type glycyl-glycine be named dipeptides and that anhydride-like combinations of a greater number of amino acids be denoted tripeptides etc." This appears to mark the introduction of the word *peptide* into the language of chemistry. In subsequent publications Fischer also began to use the term *polypeptide*.

In the abstract Fischer also wrote:

Finally the speaker discussed the coupling of the amino acids in proteins. The idea that acid-amide-like groups play the principal role most readily comes to mind (*liegt am nächsten*), as Hofmeister also assumed in his general lecture this morning. The same conviction led him [Fischer] more than 1½ years ago to initiate experiments to effect the synthetic linkage of amino acids.

The last sentence was clearly intended to draw attention to Fischer's paper on the synthesis of glycyl-glycine and its derivatives.[14] I will consider more fully later in this essay Fischer's efforts in the peptide field, and their relation to his views on the structure of proteins.

The Karlsbad meeting that links Hofmeister and Fischer thus provides still another apparent instance of simultaneous scientific discovery.[15] For the purposes of this essay, however, their encounter is of greater interest in offering a contrast in the style of two scientists with different backgrounds and personalities, who worked in different institutional settings, and who had met in the consideration of the same scientific problem.[16] The biologist Hofmeister had already done extensive and important work on proteins, and held a large view of the role of chemistry in the study of physiological problems. The chemist Fischer had just entered the arena of protein research, and was emboldened by his notable success in the synthesis of sugars and purines to believe that synthetic organic chemistry could also solve the problem of protein structure. In scientific stature, as measured by public esteem, Fischer vastly overshadowed Hofmeister. At the time of the Karlsbad meeting Fischer already held the title *Geheimer Rat*,[17] and a few months later he was awarded a Nobel Prize in Chemistry, whereas Hofmeister received no honors of this sort. Also, in the hierarchy of the university disciplines in Wilhelmine Germany (as indeed elsewhere), organic chemistry had a far higher status than did physiological chemistry, in part because of the service of academic organic chemistry to the growing chemical industry, and in part because of the domination of physiological chemistry by the clinicians and physiologists in the medical faculties. During the first decade of this century, despite the differences in their public prestige, Fischer and Hofmeister both exerted a major influence on the subsequent transformation of "physiological chemistry" into

a "biochemistry" less subservient to academic medicine.[18] This influence came not only from the research achievements in their respective laboratories but also from the experience gained there by young Ph.D. and M.D. students, research assistants, and guest investigators from many countries. In succeeding parts of this essay, I shall attempt to sketch the personal and scientific qualities of the two men, to examine more closely the development during ca. 1899–1914 of their common area of interest, and to compare the role of their respective research groups in the education of the next generation of productive scientists.

EMIL FISCHER (1852–1919)

Fischer's scientific career spans almost exactly the years of the first German Reich. His first published paper (in 1874) was based on the work he did for his doctorate in the laboratory of Adolf von Baeyer[19] at Strassburg, part of the booty of the Franco-Prussian War, and where the victors had transformed the university into a showcase German institution. Fischer's death in July 1919 came eight months after the capitulation of Germany in the First World War. In the bitterness of defeat, one of his eulogists wrote: "Emil Fischer represents a symbol of Germany's greatness."[20]

The number of biographical writings about Fischer is legion,[21] and for the purposes of this essay I shall only refer to some aspects of his life, work and personality that suggest something of his style as a scientist and educator. That Fischer possessed exceptional chemical talent was evident from his first publications, and the forward thrust of the German economy gave him opportunities to develop and exploit that talent in academic life and in association with a burgeoning chemical industry. There do not appear to have been any social or financial impediments to his rise to prominence, for he was neither a Jew nor a Catholic, his political

leanings were unexceptionable, and he had a wealthy father. In Baeyer's institute in Munich (Baeyer moved there in 1875 as the successor of Justus von Liebig), Fischer continued to work on dyes, the subject of his outstanding Strassburg dissertation,[22] but later published relatively few papers in this field. Instead, he chose to exploit his discovery of a compound he identified as $C_6H_5-NH-NH_2$, the phenyl derivative of the parent substance NH_2-NH_2, which Fischer named *hydrazine*. Upon the elaboration of this work, described in two long papers,[23] and their presentation as Fischer's *Habilitationsschrift* and an oral examination (gleefully recounted in his autobiography[24]) he became *Privatdozent* in 1878. In the following year came a promotion to *ausserordentlicher Professor* at Munich, and he then held full professorships at Erlangen (1882–1885) and at Würzburg (1885–1892), before he went to Berlin in 1892 as successor to August Wilhelm Hofmann.

A feature that distinguishes Fischer's reseach program in Würzburg and Berlin from those of other German university institutes of organic chemistry was his choice of problems of biochemical interest. The starting point was his discovery in 1884 that phenylhydrazine gives crystalline derivatives of natural sugars (glucose, fructose, galactose, etc.). Although Fischer did not neglect other opportunities presented by his systematic investigation of the reactions of phenylhydrazine (for example, in the synthesis of indole derivatives), the remarkable work performed by his research group on the degradation and synthesis of carbohydrates stands out, in my opinion, as the high point in his scientific career.[25] The manner in which he applied and developed the van't Hoff-LeBel concept of the asymmetric carbon atom in elucidating the stereochemistry of the sugars bespeaks the theoretical insight he brought to the problem. The methods he developed for the synthesis of sugars and their derivatives were elegant and lasting.

Although it remained for others, notably the great British school of carbohydrate chemistry (Purdie, Irvine, Haworth), to define more precisely the structure of the sugars, Fischer's achievements before 1900 represented the starting point of further investigation. And, as a by-product of his organic-chemical work was the study of the fermentation of sugars and of the cleavage of glycosides by enzymes, leading to Fischer's famous lock-and-key analogy of the specificity of enzyme action.[26]

Before initiating his work on sugars, Fischer undertook the systematic study of caffeine because he questioned the validity of the proposal made by Ludwig Medicus (in 1875) that its structure is closely related to that of uric acid. In a series of elegant synthetic experiments between 1881 and 1898, Fischer provided definitive evidence for the correctness of Medicus's views, and showed that caffeine and uric acid, as well as xanthine and guanine, are derivatives of a parent substance Fischer named *purine*.[27] During the 1880s, largely through work of Kossel, it became known that the purines guanine and adenine are constituents of nucleic acids.[28] The Nobel Prize in Chemistry awarded Fischer in 1902 was in recognition of his synthetic work on sugars and purines.

Fischer entered the protein field in 1899, and during the succeeding ten years the efforts of his research group were directed principally to the study of proteins, peptides and amino acids. This aspect of Fischer's research career will be considered later in this essay. His success fell short of his hopes, and after 1908 Fischer returned to carbohydrate and purine chemistry, attempted to enter the nucleic acid field through the synthesis of nucleotides, and initiated a sustained and successful research program on substances he termed *depsides* (Greek *depsein*, to tan), present in lichen substances and in tannins.[29]

Fischer's scientific papers and lectures were collected in eight volumes, which include approximately 600 experimental arti-

cles and about 20 lectures.[30] Of the former, 185 appeared under his sole authorship and 295 as joint publications, with Fischer's name first in all but two of them. Nearly all the remaining 120 experimental papers were published under the sole authorship of his Ph.D. students, and represent extracts from their dissertations. It appears to have been Fischer's practice to report the work he con-sidered to be important in the form of joint papers with his students, but also to allow them to have at least one independent pub-lication, apart from the dissertation. On the other hand, in the case of work done by his postdoctoral assistants, Fischer often pub-lished important papers under his sole au-thorship, with an acknowledgment to the assistant at the end of the paper.

This sketch of Fischer's scientific achieve-ments may perhaps suffice to indicate not only his exceptional chemical talent but also his ability to direct effectively the work of his research group.[31] During his first two professorships, at Erlangen and Würzburg, at any one time the group included three or four postdoctoral research assistants and a larger number (eight to twelve) of Ph.D. students, some of whom came from abroad. Many of Fischer's assistants were drawn from the ranks of his own students, and he also accepted men who had done their doc-toral work elsewhere. After his move to Ber-lin in 1892, Fischer continued to attract nu-merous Ph.D. students, and his fame also brought guest investigators. Among the latter were not only young chemists, but also young physicians who saw new opportuni-ties for medical research in the kind of or-ganic chemistry done in Fischer's institute. Moreover, Fischer had established close connections with several chemical compa-nies, and began to collect royalties from his patents.[32] These connections helped him to extract from the Prussian government a new building and sizable funds, so that he could employ more postdoctoral research assis-tants. Around 1905, his research group was composed of twenty-five to thirty assistants, students and guests. The usual length of stay of the assistants was two to three years, of the students about eighteen months, and of the guests six to twelve months.[33]

In the conduct of Fischer's successive re-search programs, the most important junior associates were his personal research assis-tants (*Privatassistenten*). They received a sal-ary from government funds assigned to Fischer or from his private purse. Among these assistants were men who held the title of *Privatdozent*, by virtue of having met the requirement for the *Habilitation* (the publi-cation of a scientific paper, a lecture on the subject, and an oral examination by appro-priate full professors). This entitled the *Pri-vatdozent* to lecture to students, from whom he was supposed to derive fees, but he re-ceived no salary for this service. Conse-quently, unless a *Privatdozent* had adequate means (as in Fischer's own case, from a wealthy father), he was obliged, while wait-ing for a "call" to a professorship, to accept employment as a research assistant. Nor did a promotion to *ausserordentlicher Professor* alter the *Privatdozent's* status so far as a gov-ernment salary was concerned.[34]

The main duty of Fischer's research stu-dents was to conduct laboratory operations involving the preparation of crystalline compounds, to study the products formed by treatment with various chemical reagents (and occasionally with enzymes), and to perform elemental analysis on the com-pounds they prepared. Whenever it was possible to grow large crystals, the students were also expected to take them to the min-eralogy laboratory and to determine their crystallographic parameters. Fischer (di-rectly, or through one of his chief associates) assigned to the research student a particular task, as part of a larger plan he had formu-lated, or to test the capacities of the student by means of a small problem not necessarily related to the main line of research at that time. There is little evidence in the Ph.D.

dissertations of a significant intellectual input on the part of the student. Indeed, as noted by his last chief research assistant, Max Bergmann, Fischer was reticent toward his coworkers

when he gave them instructions for the conduct of experiments or himself did laboratory work in their presence. Then, an indication of the purpose and goal and expected outcome of the experiment was either not given or stated very incompletely. The explanation of this behavior may be found in a printed guide for the conduct of scientific experiments, which Fischer regularly presented to the older students of his institute and to his own assistants. One sentence was: "You are urgently warned against allowing yourself to be influenced in any way by theories or by other preconceived notions in the observation of phenomena, the performance of analyses and other determinations."[35]

As one reads the doctoral dissertations of Fischer's students, one cannot but be struck by their limited scope and relatively modest contribution to chemical knowledge. To be sure, the completion of moderately difficult tasks might have been preceded by failures, and the mere performance of the elemental analyses was time-consuming, but the skimpiness of content raises questions about the educational benefits the student may have derived from his participation in a significant research program.

Descriptions of Fischer's behavior toward his junior assistants vary widely. One of his former English students wrote:

Physically commanding, his authority rested on the solid foundation of natural dignity unmarred by self-assertion. The brisk, upright carriage marked the man of action; the glowing eyes revealed his attitude of constant, keen enquiry; the impatience with trivialities was one aspect of his dominating, steadfast control of essentials. With ordinary human perception, it was impossible for anyone to escape his contagious enthusiasm, and yet all the time the master did not obscure the man, for although his daily demeanour was tinged with severity, his heart when revealed was deeply kind, and, in circumstances of relaxation, joyous.[36]

An American guest worker in 1905 later described Fischer as follows:

He was then fifty-three years old, his dark hair and beard streaked with gray. He was above medium height, erect, not portly, in his gait deliberate and elastic, yet in no sense suggestively military. He was modest, kindly, always the gentleman. Twice a day he made the rounds, moving quietly from desk to desk inspecting the work, always seeming interested, criticizing, helpfully suggesting. He had the faculty of seeing quickly where one's trouble lay. So gentle in manner was he that one scarcely realized that he was a good executive commanding officer.[37]

A somewhat different attitude is conveyed by a more recent account, based on archival and published material:

The Berlin institute was administered by Fischer in a strict and authoritarian manner. He differed in this respect from his predecessor Hofmann who, as Director of the Institute, allowed the reins to hang loosely. Punctuality was the chief command. Although he lived next to the Institute since 1900, and could reach the laboratories directly from his official residence, it is reported that Fischer usually passed through the rooms wearing a formal black hat. With a stern eye he inspected the laboratory workers, who reported to him the progress of their experiments. Fearsome was his *Flügelschlagen* (flapping of wings), without further comment, for the poor wretch if something had gone thoroughly wrong. Only rarely did the chief sit on a stool and conduct a brief private conversation. Then it was even permissible to laugh. However, the slightest attempt at intimacy would terminate the conversation immediately.[38]

In part, Fischer's personal qualities were affected by continued ill-health and, in later life, successive family tragedies. Throughout his professional career he was afflicted by respiratory and intestinal problems, arising from and exacerbated by the poor ventilation of the laboratories where he worked. His discovery of phenylhydrazine in 1875, and its frequent use thereafter, exposed him to an agent whose toxicity he recognized only about 15 years later.[39] In 1881, Fischer had

an attack of mercury poisoning, as a consequence of the generation of the volatile mercury diethyl during experiments on the reaction of mercuric oxide with alkyl phenylhydrazines. Indeed, in 1885 some members of the Würzburg faculty opposed Fischer's appointment because of his respiratory difficulties.[40] His correspondence of later years is replete with letters from various spas to his chief laboratory assistants reporting the state of his health.

To this should be added the tragic early loss of his wife Agnes (née Gerlach) whom he married in 1887. From this marriage, about which Fischer wrote with extreme reservation, came three sons: Hermann Otto Laurenz (1888–1960) who later became a distinguished organic chemist; Walter Max (1891–1915) who interrupted his medical training because of an acute depression and committed suicide; and Alfred Leonhard Joseph (1894–1917), a physician who died of typhus while on military service in Rumania. Agnes had died in 1895 as a consequence of meningitis that followed a middle-ear infection, probably (as Fischer states it) "because the life-saving operation was performed too late, on account of the opposition of the patient."[41]

Although personal illness and family tragedy must have contributed to the molding of Fischer's temperament, there can be little doubt that the dominant factor was his uncompromising singleness of purpose as a research chemist. At least until he became a public figure in 1902, with the award of the Nobel Prize, Fischer eschewed involvement in academic or governmental business that did not affect directly his research interests, although his relationship to several chemical firms had been of long standing. Also, from the accounts of his many biographers, he appears to have been indifferent to literature, music, art or other cultural distractions from his professional work.

After 1902, Fischer participated more actively in public affairs, initially (1905) in

promoting the idea of a Reich Institute for Chemistry as a counterpart of the *Physikalische Reichsanstalt* then under consideration, and later (1909) in the successful collaboration with Adolf von Harnack to persuade government and industrial leaders to establish the Kaiser-Wilhelm Society for the Promotion of the Sciences. Fischer played a decisive role in the organization of the various research institutes founded by the Society, in particular those for Chemistry in Berlin-Dahlem and for Coal Research in Mülheim-Ruhr.[42]

One of the principal arguments offered in favor of the new research institutes was the fear that Germany would lose its preeminence in research to the United States, and the establishment of the Rockefeller Institute for Medical Research in New York was cited as an ominous sign. Although Fischer conducted a friendly correspondence with several American scientists (notably Theodore W. Richards), he declined repeated invitations to visit the United States, pleading ill-health. There also appears to have been some animus in his attitude toward Americans, as is suggested by the following excerpt from a letter to his former associate Abderhalden:

. . . I consider it likely that because of their greater wealth the Americans will beat us in several fields, and I have expressed this opinion at every opportunity. However, we can withstand this competition for a time because of our greater inventiveness and more distinguished individual achievements. That the gentlemen in America are also rather presumptuous is nothing new to me, but one can defend oneself against this at a suitable opportunity. As soon as I find the time, I will discuss this question in a retrospect on chemical research on proteins during the past 10 years.[43]

Upon the outbreak of the First World War, Fischer joined 92 other leading members of the German cultural establishment in signing the notorious *Aufruf an die Kulturwelt* of 4 October 1914, disputing German responsibility for the outbreak of war, defending the invasion of Belgium and denying the reports

of German atrocities there.[44] Although Fischer did not abandon research, the work of his laboratory proceeded on a greatly reduced scale owing to the shortage of personnel, and he was obliged to accept women as research students. Because of his scientific eminence and close relations to the German chemical industry, he became involved in the work of numerous war committees, and headed several of them.[45] In the last years of the war Fischer, along with other signers of the *Aufruf*, became increasingly despondent about the prospect of victory. In his last letters are expressions of hope that a firm and respectable government might be established in a defeated Germany, and that a socialist revolution might be averted.[46]

FRANZ HOFMEISTER (1850–1922)[47]

Hofmeister's scientific work began in Prague, where he was born the son of a well-regarded prosperous physician, and where he attended its ancient university at a time when the German-Austrian influence was predominant.[48] As a medical student, Hofmeister came to the attention of the professor of physiology, Ewald Hering, who suggested that Hofmeister should work with Hugo Huppert, whom Hering brought to Prague in 1872 to be professor of applied medical chemistry.[49] Huppert had been a student of Carl Gotthelf Lehmann (1812–1863), whose treatise on physiological chemistry had considerable influence, and who had introduced the term *peptone*, which figures largely in the story of the peptide theory of protein structure. Indeed, Hofmeister's unpublished *Habilitationsschrift* in 1879 dealt with the analysis of preparations of peptones. At that time, and for about twenty years afterward, peptones were considered by physiologists to be the final products of the degradation of food proteins in the mammalian digestive tract, and it was thought that after absorption into the blood the peptones are converted into blood proteins.[50] In 1881, the Prague medical

faculty decided to establish a new institute of pharmacology, with Hofmeister as its chief, so he had to obtain a *Habilitation* in the subject. Two years later he spent six months in Strassburg, where Oswald Schmiedeberg headed the leading German institute of pharmacology.[51] There can be little doubt that this visit, apart from introducing Hofmeister to the teaching of pharmacology, greatly broadened his scientific outlook and also played a significant role in his later appointment at Strassburg.

During his years as full Professor of Pharmacology at Prague (1885–1896), Hofmeister and his junior associates worked on a variety of biochemical and physiological problems. An empirical study of the ability of various inorganic salts to precipitate proteins led him to discover in 1888 a regular order, which later came to be known as the "lyotropic series" or "Hofmeister series." He recognized that the differences among inorganic salts in the "salting-out" of proteins was a general function of their hydration, but did not write of ions; Svante Arrhenius's theory of electrolytic dissociation was not widely accepted until the 1890s. An important consequence of Hofmeister's systematic study was his use of ammonium sulfate (introduced into protein chemistry by Camille Méhu in 1878) to effect the crystallization of egg albumin; this approach to the purification of proteins was actively pursued in Hofmeister's laboratory and was taken up by many other investigators.[52] Hofmeister also examined the swelling and adsorption phenomena exhibited by proteins, of interest to many nineteenth-century biologists in relation to the properties of protoplasm; these phenomena were later studied extensively from the point of view of the new colloid chemistry.[53] Apart from the chemical work on proteins and peptones, Hofmeister and his associates in Prague made contributions to the study of several aspects of intermediate metabolism. Much effort was devoted to the fate of peptones in various animal tissues; the finding

that peptones (as measured by the biuret reaction) disappear in the intestinal tract raised questions about the so-called peptone theory of protein synthesis. Hofmeister's associate Julius Pohl examined the oxidation of alcohols and fatty acids in the animal body,[54] and Hofmeister himself contributed to the study of the newly-discovered process of biological methylation and of the long-fashionable problem of urea formation.[55] Until his departure from Prague in 1896, Hofmeister and his junior colleagues published about 75 papers on protein chemistry, intermediate metabolism, and assorted other topics in biochemistry, physiology and pharmacology. Only 30 of these publications bear Hofmeister's name, and most of them were based on work he has done at the beginning of his scientific career.[56] It is also noteworthy that much of the output of Hofmeister's Prague laboratory served as background for the independent efforts of his new junior associates in Strassburg.

In 1895, the chair of physiological chemistry at Strassburg became vacant, owing to the death of Felix Hoppe-Seyler.[57] It would hardly be appropriate to say that this full professorship was the most prestigious one in its field in Germany, because there was only one other, in Tübingen, whence Hoppe-Seyler had come to Strassburg in 1872, when it was made a showcase German university. In contrast to Tübingen, the Strassburg institute was in the medical faculty, and its senior members proceeded to seek a replacement. According to the archival records in Strasbourg,[58] Schmiedeberg was placed in temporary charge, and the post was offered to Gustav Hüfner of Tübingen, who was highly regarded for his work on hemoglobin. He declined on 12 December 1895, and gave his advanced age as the reason, but a later biographer stated that Hüfner did not wish to join a medical faculty.[59] The post was then offered to Eugen Baumann, Professor of Chemistry at Freiburg in Breisgau, who had made several noteworthy discoveries in the

study of the chemistry and metabolism of amino acids. He declined the Strassburg offer on 18 February 1896 because he did not wish to leave his chemical laboratory.[60]

The Strassburg medical faculty then proposed that physiological chemistry only have an *ausserordentlicher Professor* within an institute of hygiene and bacteriology (which Hoppe-Seyler had also represented), for which the Amsterdam professor Josef Förster (1844–1910), a member of the Voit-Pettenkofer school, had been proposed. Indeed, the Strasbourg archives contain a copy of a memorandum (25 February 1896) to this effect from the Curator of the University to Förster. At this point, some of the original 1872 faculty, notably the pharmacologist Schmiedeberg and the physiologist Friedrich Goltz, intervened. According to Hofmeister's associate Spiro,[61] these two men "immediately asked an audience with the Governor, Count Hohenlohe, and explained to him that because of the extensive space that had been allotted to Hoppe-Seyler, the establishment of two separate full professorships with separate institutes was possible without any new construction and without additional cost." Their argument proved to be persuasive, and no doubt owing to the influence of Schmiedeberg, Hofmeister was offered the chair of physiological chemistry. He accepted it on 23 June 1896, and took up his duties later that year. Spiro takes occasion to note the generosity of Schmiedeberg's attitude toward Hofmeister, since the two men had similar research interests in the study of metabolic problems.

I have described the circumstances of Hofmeister's appointment because it suggests something of the attitude of the Strassburg medical professors toward the discipline that Hoppe-Seyler had represented, and also toward Hofmeister as an incoming colleague. The relatively meager archival record of his relation to the administrative officers of the medical faculty during 1896–1918 gives hints, but no more, of difficulties with regard

to the appointment of teaching assistants and the like.[62] Whatever future historical study may uncover about Hofmeister's institutional problems, the circumstances of his appointment alone suggest a situation repeated later in many medical schools in many countries. With few exceptions, for the clinical professors and professors of physiology who controlled the medical faculties of German universities, biochemistry (as it came to be called) was considered to be useful in medical education and research only as part of physiology or in relation to its application to practical clinical problems.

During the 22 years of Hofmeister's stay at Strassburg, approximately 300 papers were published from his institute. A noteworthy feature of the list is that only about fourteen bear Hofmeister's name. Among this small number there were several general articles that attracted wide interest. I have already mentioned the two on the structure of proteins that appeared in 1902, and there was another on this subject in 1908.[63] Also, in 1901, Hofmeister published a small brochure which dealt with the integration of enzyme action in metabolic processes. Some historians of science have considered this publication to have been influential in the emergence of a modern biochemistry based on the enzyme theory of life.[64] Thirteen years later, Hofmeister wrote another article in which he modified his views on this subject in line with the then-current ideas about the colloidal nature of living matter.[65] In 1912, he published a lecture on chemical regulation in the animal body, and nearly all of his succeeding papers dealt with problems of nutrition,[66] with particular attention to what he called "accessory nutrients" (Frederick Gowland Hopkins had termed them "accessory food factors" and Casimir Funk "vitamines"). Thus, in the scientific literature after 1900, Hofmeister's name appeared principally as the author of general surveys of various important biochemical problems.

The significant experimental papers from Hofmeister's Strassburg institute were published under the sole authorship of his assistants, students (mostly candidates for the M.D. degree), and postdoctoral guests. These papers represented a wide range of interest, in keeping with Hofmeister's opinion that "The elucidation of the most fundamental physiological questions depends above all on progress in three fields accessible only to the chemist: protein chemistry, enzyme action, and intermediate metabolism."[67] In all these fields, his Strassburg research group made sterling contributions and, as noted before, several of them were elaborations of work done in his Prague laboratory.

Hofmeister's chief associate in Strassburg was Karl Spiro, who joined him in 1896, and remained with him until they both left in 1919. After his work for the Ph.D. (1889) in organic chemistry with Emil Fischer, Spiro studied medicine at Breslau (M.D. 1893) and turned to pharmacology. This brought him to Schmiedeberg's institute in Strassburg; upon the arrival of Hofmeister, Spiro became his first assistant, and embarked on a sustained study of the physical-chemical properties of proteins. There can be little doubt that Hofmeister's earlier work in this field stimulated Spiro's productive efforts. Of special historical interest is his 1914 paper, with Max Koppel, on buffers.[68] Other notable contributions of the Strassburg group to protein chemistry included the application of the salting-out method to the crystallization of human serum albumin (Hans Theodor Krieger, 1899) and of Bence-Jones protein (Adolf Magnus-Levy, 1900) as well as the isolation of thyroglobulin (Adolf Oswald, 1899). Moreover, a study by Spiro and Otto Porges on the fractionation of serum proteins led to their discovery that at least three types of globulins are present, and foreshadowed the demonstration many years later of the identity of the so-called gamma-globulin fraction with the immunoglobulins. Among the other achievements in the protein field, that of Ernst Friedmann

in establishing the structure of the amino acid cystine is especially noteworthy, as it corrected the widely-accepted formula previously proposed by Baumann.

The successes of the Strassburg group in the field of enzyme action were perhaps not as striking, but the discovery by Jacob Parnas of the enzyme he named "aldehyde mutase" deserves special mention.[69] Other enzyme studies dealt with tyrosinases (Otto von Fürth), and several of Hofmeister's associates examined the properties of proteinases; in particular, Julius Schütz's work on the kinetics of pepsin action later attracted considerable attention. It is perhaps fair to say that the greatest single success was made in the field of intermediate metabolism, with Franz Knoop's demonstration of the β-oxidation pathway for the metabolic breakdown of fatty acids.[70] Also, it was in the Strassburg laboratory that Parnas began his fruitful studies in the field of intermediate carbohydrate metabolism. In addition to these contributions to the three areas of biochemical endeavor mentioned by Hofmeister in 1900, there were also incisive studies on other topics, for example Otto von Fürth's work on the constitution of adrenalin, Friedrich Bauer's important study on the structure of inosinic acid, and Wilhelm Stepp's discovery of what was later to be called fat-soluble vitamin A.

The remarkable variety of research problems attacked in Hofmeister's Strassburg institute precludes a complete summary of the research of his junior associates. It is clear, however, that this beehive of fruitful activity did not represent a concerted group attack on particular problems along lines determined by the leader. From the published recollections of several of Hofmeister's associates, and from obituary notices about them, there can be little doubt that instead of assigning problems, he suggested them, and that he also helped significantly both in the conduct of the work and in the preparation of papers for publication.[71] The available records suggest that the Strassburg

group included at any one time about 20 people, of whom two or three were salaried assistants; some of them held the title of *Privatdozent* or, as in the case of Spiro, of *ausserordentlicher Professor*. The other members of the group appear to have been equally divided between research students who were candidates for the M.D. degree and post-doctoral (mostly post-M.D.) workers, some of whom held assistantships in other medical school departments. The average size of Hofmeister's Prague group is uncertain, but presumably it was smaller than the one in Strassburg.

Not all of Hofmeister's suggestions led to publishable results. Lawrence J. Henderson, who was at the Strassburg laboratory during 1902–1904, wrote thirty years later;

The experimental problem on which I went to work within a few weeks of the opening of the semester, after I had satisfied Hofmeister that I possessed a very rudimentary skill in chemical work, was badly chosen. I remember saying to him at the outset that I should like to work on some problem about blood and I also remember that this was due to a clear perception that I was going to work on the acid-base equilibrium in blood at some time when I returned to America. But although Hofmeister had himself done important physico-chemical work I willingly accepted his proposal to study the products of partial hydrolysis of hemoglobin and on this problem I worked steadily throughout my first year in Strasbourg and intermittently throughout my second year, without ever making any progress, so that nothing ever came of my experimental work during these two years. And yet, strange to say, during all this time I was happy, contented and, I think, never seriously disturbed at the failure of the investigation. . . . I was for the first time surrounded, at least during the working hours in the laboratory, by a group of active young biological chemists, the assistants Spiro and Fürth, and in addition, Embden, Knoop, Friedmann, Blum and others. Then, Hofmeister's lectures were excellent and, considering his age and lack of training, remarkably modern and adequate to the needs of the immediate future. Moreover, he was not merely a chemist, for he possessed a real understanding of at least some of the com-

plexities of biological phenomena and therefore of the characteristic difficulties in the application of physical and chemical methods to their study.

In 1908, Henderson spent a month in Strassburg:

Spiro and I did two little pieces of experimental work in cooperation. This work arose from his remark that it was a pity that I had never published anything from the Strasbourg laboratory and that we ought each to propose a problem that could be finished in a month and work both out, and so we did. The problem I proposed was an uninteresting routine measurement, but Spiro suggested the physico-chemical explanation of the long-known phenomena of the movement of water and of chloride ion between cells and plasma when the pressure of carbon dioxide in blood is varied. For some reason that I can't explain, I had up to that time overlooked these facts. I was the more impressed by them because I felt guilty at my ignorance. There was no difficulty in formulating the theoretical explanation of the facts through an application of the theory of acid-base equilibria and of the theory of osmotic pressure. The problem having been thus clarified, it was easy to construct simple systems in which the same processes should be observable, and, having performed the experiments, we found what we were looking for.[72]

The scope of the research done by Hofmeister's group, and the manner of its publication, suggests an attitude quite different from that of Fischer to the assignment of credit. This is consistent with the available accounts of Hofmeister's personal qualities. In his obituary notice about Knoop, Karl Thomas wrote of the lifelong reverence and gratitude Knoop bore toward Hofmeister, "a man of wide-ranging spirit full of new ideas that he generously handed out to his co-workers"; and similar sentiments may be found in articles about other former junior associates, for example the botanist Friedrich Czapek (who worked in Hofmeister's Prague laboratory), the pharmacologist Alexander Ellinger, the clinician Gustav von Bergmann, and the biochemists Gustav Embden, Ernst Friedmann and Henry Stanley Raper.[73] Otto

Loewi, who worked in the Strassburg institute in 1897, later described Hofmeister as "an ingenious biologist and an unforgettable personality," and credited him with guiding Loewi on a path in pharmacology that led him to Hans Horst Meyer, in whose laboratory Loewi made the first of his two great discoveries.[74] Moreover, in the face of the tension between the German rulers and the French population of Alsace, Hofmeister won the affection of his Alsatian students, and made special efforts to promote their interests.

Hofmeister appears to have been a man of good humor and great energy, as well as a "sparkling conversationalist, full of the grace of the Austrian." Also, he had a happy family life and, until shortly before his death, enjoyed good health. There were leisure hours spent in doing watercolors or listening to music. But at root, according to Spiro, he was "a solitary person, who desired solitude, . . . and he regarded the world around him with complete skepticism and often with scorn."[75] This is consistent with Hofmeister's avoidance of scientific meetings, except when he was invited to present a lecture. In this connection it is of interest that Emil Abderhalden, who attended many meetings at which physiological chemists were present, wrote that he had never met Hofmeister.[76] It would seem, therefore, that although Hofmeister was energetic within his institute, he was not an active participant in the academic politics of Wilhelmine Germany and received few public honors. His last years were sad ones. After the return of Strasbourg to French rule, he left with the German professors, and found a haven in Würzburg, where he was named Honorary Professor of Physiological Chemistry. In a laboratory provided by the Professor of Pathology, Martin Benno Schmidt, Hofmeister worked alone on the isolation of the antineuritic vitamin until shortly before his death on 26 July 1922.[77]

In assessing Hofmeister's scientific contributions, it is noteworthy that a recurrent

theme in the writings about him is that he saw biochemical problems with the eyes of a biologist.[78] I cannot dispute this judgment, but I find a curious paradox. Whereas Hofmeister considered the proteins that he and his coworkers had crystallized to be discrete substances of high molecular weight, the chemist Fischer did not. For this reason, I now return to the problem both scientists considered at the 1902 Karlsbad meeting, with special reference to Fischer's role in the historical development of protein chemistry.

PEPTIDES, PEPTONES AND PROTEINS

On January 6th I will present a lecture at the Chemical Society summarizing my work on amino acids, polypeptides and proteins, and then early next year I will publish the collected papers in this field in the form of a book. The material has grown splendidly and there is much detail in it. Recently I have also prepared the first crystalline hexapeptide and hope to obtain a matching octapeptide before Christmas. Then we should be close to the albumoses. Unfortunately, then begin the principal difficulties, namely the identification of the artificial products with the cleavage products of proteins. . . . My entire yearning is directed toward the first synthetic enzyme. If its preparation falls into my lap with the synthesis of a natural protein material, I will consider my mission fulfilled.

So wrote Emil Fischer to Adolf von Baeyer on 5 December 1905; the text of the January 6 lecture and the promised book appeared during 1906.[79]

In the lecture, Fischer first summarized the work of his research group on the isolation of optically-active amino acids by resolution of amino-substituted derivatives of the available racemic forms; this represented Fischer's entry into the protein field in 1899, and successive students were subsequently assigned the task of applying his method to the resolution of many synthetic racemic amino acids, some of which were first made in his laboratory.[80] After a description of the synthesis and properties of various amino acid derivatives, Fischer turned to the polypeptides, and stated that he had expected from the start such artificial substances would resemble the peptones.

As was noted previously in this essay, Fischer's peptide work began in 1901, with the preparation of the first free peptide—glycyl-glycine—by partial hydrolysis of glycine anhydride (2,5-diketopiperazine), a compound made by Curtius during the 1880s. This is not a general method for coupling amino acids to form polypeptides, and Fischer's first attempt to develop such a procedure failed. The later development of peptide chemistry showed that his proposed strategy of blocking the amino group with a substituent that could be selectively removed at the end of the peptide synthesis was sound, but the substituent he chose (the carbethoxy group, C_2H_5OCO-) proved to be unsuitable. It was not until 1903 (after the Karlsbad meeting) that he described a procedure that circumvented the need for an amino-protecting group. In the new method, the synthesis began with a halogenacyl halide (e.g., $Br(CH(R)CO-Cl$). This was coupled to an amino acid derivative ($NH_2CH(R')CO-X$) to yield a compound of the type $BrCH(R)CO-NHCH(R')CO-X$, which was then converted by means of ammonia into the dipeptide derivative. Treatment of this product with the bromoacyl halide derived from another amino acid gave, after amination, the expected tripeptide derivative, and so on. By 1906 about 65 peptides of different chain length and amino acid composition had been made in this way by various members of his research group; three years later the total exceeded 100, the longest being an octadecapeptide with 15 glycine and 3 leucine units. At each stage of the investigation, the synthetic peptides were subjected to the tests devised earlier by physiological chemists to study proteins and their enzymatic breakdown products—the biuret reaction, precipitation by inorganic salts, cleavage by proteolytic enzymes. From such

tests Fischer concluded that the lower members of the series resembled the peptones and that, as the chain length increased, the properties of the synthetic materials began to approach those of natural proteins.

Fischer was not reticent in his claims for the power of his synthetic procedure:

The synthesis of the higher terms (peptides) has been restricted hitherto to the combinations of glycine, alanine and leucine; there is not a shadow of doubt, however, that all the remaining amino acids could be associated in complicated systems with the aid of our present methods. The knowledge of the artificial polypeptides thus acquired has opened up new ways of investigating the peptones and albumoses analytically. During more than fifty years physiological chemists have endeavored without much success to isolate homogeneous substances from these ill-defined materials; all the products described by them, however, bear indubitable evidence of being mixtures.[81]

Fischer's confidence in the power of his synthetic method proved to be short-lived, for it was not only cumbersome and costly, but also was unsuitable for the preparation of polypeptides containing more complex amino acid units, for example lysine or glutamic acid. The enormous effort of his assistants and students produced much less than he had hoped for, and his disappointment may be inferred from the fact that after 1910 there were no further experimental publications on peptide synthesis from his laboratory. Fischer's halogenacyl halide method became obsolete when he ceased to use it, and only survived in the laboratory of Emil Abderhalden in Halle, where many peptides were produced, albeit of uncertain identity or purity. Among them was a nonadecapeptide containing one more leucine than Fischer's longest polypeptide. It may be added that less attention was paid during 1900–1910 to Theodor Curtius who, stimulated by Fischer's entry into the protein field, resumed his work on peptides and developed in 1902 a coupling method involving the azides of

acylamino acids; this procedure has been used fruitfully to this day, and the historical significance of Curtius's contributions to the development of peptide chemistry is now appreciated more fully.

Whatever may be said about the many practical limitations of Fischer's method, and its rapid obsolescence, they do not diminish his decisive role in providing an impetus to later advances in the art of peptide synthesis. The high point came in 1932, with the invention of the so-called carbobenzoxy method by Max Bergmann and Leonidas Zervas.[82] Their procedure is an ingenious modification of Fischer's unsuccessful use of the carboethoxy group, and made possible the facile synthesis of polypeptides containing all protein amino acids. In addition to Fischer's general influence on the subsequent development of peptide chemistry, special mention must also be made of a by-product of the work on the halogenacyl halide method. Since proteins are composed of amino acids which, with the exception of glycine, have a center of asymmetry and are optically active, it was necessary to prepare the halogenacyl halides from optically-active amino acids. This process led to an inversion of configuration about the center of asymmetry, and the inversion was reversed upon treatment of the halogenacyl peptide with ammonia at the final stage of the synthesis. This type of double inversion had been discovered in 1893 by Paul Walden, but Fischer's work between 1907 and 1911 shed new light on the process and gave evidence of the remarkable stereochemical insight that he had displayed earlier in his work on sugars.

The final section of the 1906 lecture dealt with proteins, and began with a detailed description of the method Fischer had devised in 1901 for the amino acid analysis of protein hydrolysates, namely the fractional distillation of amino acid esters under reduced pressure. Many protein preparations were subjected to such analysis and, apart from

the detection of previously-known protein constituents, three new ones were added to the list: proline, hydroxyproline, and diaminotrioxydodecanic acid. Much of this work was done by Emil Abderhalden, in association with a series of guest investigators, largely young M.D.'s.[83] Fischer then discussed experiments (also largely performed by Abderhalden) on the partial cleavage of proteins by proteolytic enzymes, especially those present in "pancreatin" (at that time, the term "trypsin" was also applied to this enzyme preparation). He reported the isolation of glycyl-alanine diketopiperazine from a partial hydrolysate of silk fibroin, and withdrew his earlier claim (in 1902) for the isolation of glycyl-alanine in the form of an amino-substituted derivative. In subsequent publications (1907), Fischer reported the isolation of other small peptides from protein hydrolysates.

Fischer concluded his lecture with a discussion of the structure of proteins, and stated that "So far as I can judge, the prevalent view is that in protein molecules the amino acids are joined by amide bonds. This idea was most fully treated by Hofmeister, but he will surely not claim to be its originator, for all synthetic efforts to couple amino acids, among them the discovery of glycylglycine, which antedate his publication, are based on this assumption. . . . I wish however to note that simple amide formation is not the only possible mode of linkage in the protein molecule. On the contrary, I consider it to be quite probable that on the one hand it contains piperazine rings, whose facile cleavage by alkali and reformation from the dipeptides or their esters I have observed so frequently with the artificial products, and on the other hand the numerous hydroxyls of the oxyamino acids are by no means inert in the protein molecule. The latter could be transformed by anhydride formation to ester or ether groups, and the variety would increase further if poly-oxyamino acids are assumed to be probable protein constituents.[84]

Apart from his ambivalent commitment to the peptide theory of protein structure Fischer also took a stand against the evidence that proteins have molecular weights greater than 4,000–5,000. He stressed his opposition repeatedly; for example, in his Faraday Lecture he stated: ". . . l-leucyl-triglycyl-l-tyrosine has all the properties of the albumoses. These observations are of importance as casting doubt on the view which formerly prevailed that, being intermediate products between proteins and peptones, the albumoses are substances of considerable complexity." Later in the same lecture, Fischer voiced the hope that, by means of his method, he would be able to synthesize silk fibroin, which he considered to be one of the simplest proteins, and went on to say: "To deal with the whole of the proteins will be a gigantic task; so large a number of separate investigations will be necessary that nothing less than the life-work of a whole army of inventive and diligent chemists will suffice to complete it. Probably, too, the unpleasant discovery will be made that the natural proteins as we know them today are only to be obtained by mixing the homogeneous artificial products."[81] This theme recurred in his correspondence; for example, in a letter to Lewellys F. Barker, Fischer wrote: "The synthesis of polypeptides is advancing briskly. I have recently made the first decapeptide and will now try to reach an eikosapeptide, whereupon one should be midway in the protein group."[85]

In 1913, Fischer reported the synthesis of a depside derivative having a molecular weight of 4,021. This led him to state that this value exceeds that of the octadecapeptide he had described in 1907 by a value of 3, and he added: "I believe that it also exceeds that of most natural proteins."[86] Three years later, in commenting on the value of 15,000–16,000 cited by Hofmeister in 1902 for the molecular weight of hemoglobin, Fischer wrote:

In my opinion, the methods applied to the determination of the hemoglobins are less certain than

had been assumed previously. Although they crystallize beautifully, no guarantee of homogeneity is given, and even if one concedes this and accepts the validity of a molecular weight of 15,000–17,000 for several hemoglobins, it should always be remembered that the hematin, from all that we know of its structure, can bind several globin units. . . . On the other hand, I gladly concur in the view of Hofmeister and other physiologists that proteins of molecular weight 4000–5000 are not rare. If one assumes an average molecular weight of 142 for the amino acids, this would correspond to a content of 30–40 amino acids.[87]

It is difficult to escape the surmise that Fischer's views about the molecular weight and homogeneity of crystalline proteins had at root the realization that acceptance of the claims of the physiological chemists would imply his concession that, despite his repeated assertions to the contrary, his method of peptide synthesis was inadequate to solve the problem of protein structure. Indeed, this conclusion is implicit in an article by Hofmeister, published in 1908. He began by noting: "That the end products (of protein hydrolysis) are largely linked to one another as amides was concluded by me on the basis of chemical and physiological evidence, and was securely established by E. Fischer through the preparation of such compounds—the peptides." Hofmeister then called attention to the fact that "the enzymatic breakdown of proteins always leads to mixtures of many substances of unequal molecular size. . . . and the isolation of definite chemically-characterized albumoses or peptones is a thankless task. . . . The difficulty of such research is a direct consequence of the size of the protein molecule," and he goes on to cite the case of hemoglobin, for which analytical determinations of the iron content had given a molecular weight of 15,000–16,000. Hofmeister then summarized the efforts of physiological chemists, including those of several of his junior associates, to isolate individual peptones in the form of acyl (for example, β-naphthalene-sulfonyl) derivatives, noted that chemically-homogeneous products could not be obtained by the precipitation methods available at that time, but reiterated his conviction that the isolation of well-defined cleavage products was the most important requirement for the determination of the structure of proteins. Also, he did not fail to add that: "The rapid progress made in the synthesis of polypeptides under the aegis of Fischer could lead to the view that one may expect the elucidation of protein structure to come entirely from this approach. This hope at once comes to naught if one considers the enormous number of synthetic possibilities."[88]

A contributing factor in Fischer's skepticism about the available values for the molecular weight of proteins may have been his indifference to data from osmotic-pressure measurements or the determination of freezing-point depression. These methods represented some of the important contributions of the new physical chemistry, and before 1910 gave values (later shown to be too low) of 14,000 for egg albumin and 48,000 for hemoglobin. In this connection it is of interest that Wilhelm Ostwald, the chief propagandist for this branch of chemistry, later wrote about his encounter with Fischer at the 1889 meeting of the *Gesellschaft der deutscher Naturforscher und Ärzte* in Heidelberg:

I found myself in a swarm of organic chemists gathered about Emil Fischer, already regarded as the future leader of our science, since what was not organic chemistry was not recognized as chemistry. In response to his remark about our new direction I replied that organic chemists owe us thanks for the possibility of determining the molecular weights of non-volatile substances. Fischer replied "That is entirely unnecessary; I see directly the molecular weight of every new substance, and do not need your methods."[89]

It should be noted however that Fischer later promoted the development of physical chemistry in Berlin, and had high regard for van't Hoff and Nernst, but clearly his relations with Ostwald were not cordial.

I have dwelt on Fischer's work and writings about proteins because during 1900–1910 they dominated discussion of this field. The accounts of his 1906 lecture in newspapers and in popular science journals encouraged the belief that the preparation of synthetic proteins was around the corner and, although Fischer attempted to disclaim responsibility for the exaggerations, his embellishment of the biological significance of his peptide work could not fail to attract wide attention and increase his already considerable public prestige.[90] It is small wonder, therefore, that in the opinion of his contemporaries, Fischer's repeated disparagement of the efforts of physiological chemists represented expressions of sound scientific judgment. Thus, despite his notable contributions to biochemical knowledge, Fischer's role in the emergence of biochemistry as a university discipline was in part a negative one. What Fischer failed to see, or did not wish to acknowledge, was that physiological chemists had to resort to every available method, including not only organic-chemical but also physical-chemical and biological methods, to study such difficult problems as protein structure, enzyme action and intermediate metabolism. This diversity of experimental approach, evident in the work of the Hofmeister group, stood in sharp contrast to the highly-disciplined methodology of the organic-chemical laboratory. In this connection it is perhaps worth noting that in his autobiographical memoir, prepared during the 1930s, Lawrence J. Henderson wrote of his time with Hofmeister:

No doubt Hofmeister and others in Germany, and an occasional more or less isolated investigator like Hopkins in England were at that time masters of a body of knowledge differing materially from what passed as either chemistry or physiology and which might fairly be called biological chemistry. But unlike organic chemistry and physical chemistry, biological chemistry did not possess and indeed hardly possesses today a sufficient equipment of methods of its own to make possible the

sort of disciplined training that has been so long characteristic of organic chemistry and in a measure of physical chemistry. . . . Further, I have always had a feeling that organic chemistry is a very peculiar science, that organic chemists are unlike other men, and that there are few occupations that give more satisfaction than masterly experimentation along the old lines in this highly specialized science.[91]

These thoughts invite consideration of the question whether, in the description of a scientific discipline, priority should be given to the problems it seeks to solve or to the methods it uses to solve them. A corollary question is whether greater attention to problems makes for better education and concentration on methods for better technical training.

Fischer's attitude toward his contemporaries in physiological chemistry is indicated in his comments about Emil Abderhalden, who joined Fischer's research group in 1902, after receiving his M.D. in Basel, and working there with the physiological chemist Gustav von Bunge. Two years later, in a letter to his Berlin colleague, the physiologist Theodor Wilhelm Engelmann, Fischer wrote:

Because of his unusual capacity for work, in a short time Abderhalden has become so adept in the difficult methods of organic chemistry that I was able to accept him last fall as a collaborator in my private laboratory. I note that I had not dared to do this before with a medical man. He is a good observer, and is an enemy of all superfluous hypotheses. Regrettably, biological chemistry is that part of our science in which imprecise and incomplete experiments are often heavily padded with the dazzling ornamentation of so-called ingenious reflections to produce pretentious treatises. For this reason, people like Abderhalden are needed. . . .[92]

THE FISCHER AND HOFMEISTER RESEARCH GROUPS

If, as the available record suggests, Emil Fischer directed his research group rather autocratically and Franz Hofmeister's role was more like that of a senior counselor, can

this contrast in styles of leadership be attributed solely to the difference in the personalities of the two men? Certainly, an additional important reason was the fact, noted by Lawrence J. Henderson, that by the turn of the century organic chemistry had a much more distinctive and highly-specialized methodology than did physiological chemistry. This made for more disciplined training not only in Fischer's institute but also in other large organic-chemical laboratories, such as those of his teacher Adolf von Baeyer and of Fischer's student Ludwig Knorr. Moreover, the division of labor among numerous assistants and students made it possible for the leader to explore several approaches and to get many experiments done. To this may be added the fact that the higher institutional status of organic chemistry in Wilhelmine Germany conferred upon leading organic chemists like Fischer greater prestige than that accorded a leading physiological chemist like Hofmeister. The extent to which such public esteem was reflected in the way a chemist directed the work of his junior associates could not but depend on his personal qualities and ambitions. In the case of Fischer, at least during his work on proteins, the attainment of high honors does not appear to have diminished his desire for additional glory to be gained from the closely-directed efforts of his research group.

On the other hand, Hofmeister's style of leadership at Strassburg was appropriate in an emergent field whose many problems came largely from mammalian physiology. In addition to his more modest personal aspirations, Hofmeister imitated in many respects his predecessor Hoppe-Seyler and especially Carl Ludwig (1816–1895) whose Leipzig institute provided the seedbed for the subsequent development of physiology in many countries, notably in Russia, and to a lesser degree in England and the United States.[93] It is noteworthy, however, that Hofmeister's contemporary Kossel appears to have directed a sizable biochemical group

in his Heidelberg institute of physiology rather strictly, with little opportunity for independent work by his junior associates.[94]

Whatever may be said of the possible reasons for the difference in the styles of leadership of the Fischer and Hofmeister groups, the question posed at the beginning of this essay remains: If an important function of a research group is not only to produce new scientific knowledge, but also the next generation of productive scientists, what comparison can be made between these two groups with regard to the later distinction of their progeny?

Before attempting such a comparison it is useful to know something of the size and composition of each group. Such data are presented in Table 1. To collect these data for Fischer's group the starting point was the set of eight volumes of his collected papers (note 30), and a list was made of all the people whose names appeared as authors, co-authors, or recipients of Fischer's thanks for assistance in the investigation. Among the last-named individuals was Walter Axhausen, who performed the widely-hailed synthesis of the octadecapeptide mentioned in the previous section of this essay.[95] From other sources I learned of research students, assistants and guests whose names do not appear anywhere in the collected Fischer papers. In this manner, I assembled a list of 310 junior associates who had worked with Fischer during his scientific career (see Appendix 1). Not included in this list are several people with whom Fischer collaborated on the basis of equality, for example his cousin Otto Fischer (triphenylmethane dyes), Paul Lindner (fermentation of sugars), and the physician Joseph von Mering (Veronal).[96] For the Hofmeister group, the starting point was the list of publications from his Prague and Strassburg laboratories in the obituary notice prepared by Pohl and Spiro (note 47). The completeness and accuracy of their list was checked with the aid of various abstract journals and other reference works. Again,

TABLE 1

Composition of Fischer and Hofmeister Groups 1879–1919

| | Dr. phil. | | Dr. med. | | |
	Predoct.	Postdoct.	Predoct.	Postdoct.	Total
FISCHER					
German-speaking nations	172	46*		14	232
Other nations	46	23		9	78
Total	218	67		23	310
HOFMEISTER					
German-speaking nations	2	7	41	72†	122
Other nations	4	5	7	34	50
Total	6	12	48	106	172

* Includes assistants (34) and guests (12); does not include 32 research assistants who had received their Ph.D. for work with Fischer.

† Includes assistants (12) and guests (60); does not include 6 assistants who had received their M.D. for work in Hofmeister's institute.

I found some additional junior associates and excluded the few senior individuals with whom Hofmeister had collaborated, to yield a final list of 172 people (see Appendix 2). An effort has been made to collect biographical data about all the individuals in the two lists.[97] It was not difficult to find such data for those who had established themselves in academic life or at least continued to contribute articles to scientific, medical or technical journals, but those whose names disappeared from this literature presented greater problems. If account is taken of the men known to have died soon after their doctoral work, the number of those for whom I have found biographical data thus far represents about 90 percent of the total in each of the appendices.[98]

The disparity in the size of the two groups arises from the fact that during the period 1879–1896 Hofmeister's Prague group was much smaller than that of Fischer in Erlangen, Würzburg and Berlin. Between 1896 and 1914, however, the totals were closer, with approximately 90 predoctoral and 75 postdoctoral people in Fischer's Berlin institute as compared to the approximately 40 predoctoral and 110 postdoctoral people in Hofmeister's Strassburg institute.

It is evident from Table 1 that about 70 percent of Fischer's junior associates had been Ph.D. candidates, some of whom stayed on as research assistants. The sizable number of M.D.'s who worked as guests in Fischer's laboratory are of interest; many of them were turned over to Abderhalden to do amino acid analyses of proteins. In the case of the Hofmeister group, over 90 percent were either M.D. candidates or post-M.D. associates. As regards those from countries other than German-speaking nations (Germany, Austria-Hungary, Switzerland), most of Fischer's visitors came from the United States (19 Ph.D. students, 7 post-Ph.D. and 5 post-M.D. guests) and from Great Britain (16 Ph.D. students, 4 post-Ph.D. guests). The foreign members of Hofmeister's group were drawn largely from Japan (2 M.D. students, 8 post-M.D. guests), Italy (1 post-Ph.D. and 7 post-M.D. guests), Russia (6 post-M.D. guests) and the United States (1 M.D. student, 1 post-Ph.D. and 5 post-M.D. guests).

In Table 2 I have attempted to translate into numbers the principal subsequent activity of the surviving junior people for whom I have biographical data. To avoid duplication of entries, I considered the *principal* activity to be the one in which the per-

TABLE 2

Principal Subsequent Activity of Junior Members of the Fischer and Hofmeister Groups[*]

	FISCHER		HOFMEISTER	
	German-speaking nations	Other nations	German-speaking nations	Other nations
Univ. full (*ord*) Professor	31	18	42	24
Other university ranks	10	10	13	3
Scientific research institute	5	9		
Hospital research and admin.	5	1	24	8
Private medical practice	2		26	4
Industrial res. and admin.	107	17	2	1
Government techn. depts.	18	5	2	1
Chemical consultant	15	11		
Other[†]	5	2	1	1
Total	198	73	110	42

[*] Not included in this table are persons known to have died soon after their doctoral work.

[†] Includes publishing, pharmacy, farming etc.

son had spent the largest portion of his (or her) professional life; thus a brief university appointment followed by a lengthy association with an industrial firm placed the person in the latter category. Despite the occasional uncertainty of assignment, I believe that the numbers in Table 2 allow one to draw some conclusions about the later careers of the junior members of the two groups.

It is clear that a larger proportion (43 percent) of the Hofmeister people attained full professorships, as compared with 18 percent for the Fischer group. It should be recognized, however, that apart from the post-M.D. guests most of the later full professors from the Fischer group held this rank in organic chemistry, whereas most of those from the Hofmeister group were appointed in disciplines other than physiological chemistry, notably pharmacology, physiology, internal medicine and pediatrics. This difference is in part a consequence of the more limited academic opportunities for German biochemists before the Second World War. The sizable number of former Hofmeister people who did not rise in rank above *ausserordentlicher Professor* includes individuals who held such appointments as biochemists in

medical school departments of physiology or pathology.

The third category in Table 2 refers to the men whose principal scientific activity was in research institutes not attached to universities. No Hofmeister people are represented, but those from the Fischer group include some of the most distinguished scientists in the entire list. Among the Germans or Austrians were Karl Landsteiner, Otto Warburg, Franz Fischer and Max Bergmann, and among the foreigners were Ernest Fourneau, Phoebus Aaron Levene, Walter Abraham Jacobs and Donald Dexter Van Slyke.[99] In the fourth category of Table 2 are those who later joined hospital staffs. Most of them rose to be chiefs of clinical services or heads of laboratories, and continued to publish articles in the scientific or medical literature. As is to be expected, the Hofmeister group provided a larger number to this category; here again the scarcity of academic posts for German biochemists obliged many of them to content themselves with hospital appointments.[100]

The first four categories in Table 2 thus represent the junior members of the two research groups who later continued to con-

tribute to the scientific, medical or technical literature in their specialty. Clearly, the number and quality of the publications per individual varied widely, but it is of considerable interest that only 34 percent of the Fischer group are included among these categories, as compared to 75 percent for the Hofmeister group. Except for one or two minor publications or notices of patents, the remainder of the Fischer group disappeared from the literature because of their association with industrial firms, service in government bureaus such as the Patent Office, or activity as commercial chemical consultants. As is evident from Table 2, most of those from the Hofmeister group who did not continue to contribute to scientific or medical journals had entered private medical practice.[101]

The large proportion of former Fischer associates who made their careers in industry or as commercial chemical consultants merits further comment. The precursors of the leading German firms that specialized in organic chemicals (Hoechst, Boehringer, Bayer, BASF, Kalle, Casella) had been founded around 1860 and during the succeeding decades they depended for their scientific manpower on university laboratories such as those of Baeyer and Fischer. At first the emphasis was on synthetic dyes for the textile industry, and later also on pharmaceutical products.[102] The success of these enterprises encouraged young Germans to choose organic chemistry as a profession and during 1888–1914 the increase in the number of such students was roughly proportional to the growth of the chemical industry.[103] After the First World War, this phenomenon was evident in the United States where distinguished organic chemists like Roger Adams (1889–1971) at the University of Illinois provided young Ph.D.'s to staff the research departments of a burgeoning American chemical industry.

In considering the validity of the conclusions drawn from the numbers in Table 2 it

should be noted that I have been unable thus far to ascertain the subsequent fate or activity of about 10 percent of the people in each of the two groups. In the case of the chemists of the Fischer group this may have been related to early death (especially during the First World War), entry into chemical industry or commercial consulting, or a change in professional occupation. Similarly, for the Hofmeister group, it is likely that most of those who disappeared from the scientific or medical literature became practicing physicians, although three of them (Franz Goldschmidt, Hans Theodor Krieger, Hugo Schneider) appear to have died soon after their association with Hofmeister, possibly during the war.[104] Consequently it is unlikely that data for the missing people would alter markedly the proportion of the junior members of the two groups who continued to contribute to scientific or medical knowledge after their doctorate.

The limitations of numerical data in the search for historical understanding are obvious, and the data in the tables and appendices can only serve as a background for an attempt to assess the contributions of Fischer and Hofmeister to the education of the next generation of productive scientists. If the major social function of the Fischer group was to provide research and management personnel for the growing German chemical industry, the group also included many future scientific leaders whose later achievements reflected Fischer's influence to a greater or lesser degree. The same applies to the productive progeny of the Hofmeister group, although it may perhaps occasion some surprise that they were so numerous as compared to those who became medical practitioners. To discuss individually all of the productive scientists in the two groups would increase excessively the length of this essay. I have therefore selected those who, in my opinion, gained some distinction (their names are given in the appendices in capital letters) for a consideration of the relation of

their achievements to their association with Fischer or Hofmeister.

My list of the more renowned former members of Fischer's group includes 24 names; 4 received a Nobel Prize in Chemistry (Otto Diels, Hans Fischer, Fritz Pregl, Adolf Windaus) and 2 in Physiology or Medicine (Karl Landsteiner, Otto Warburg). Since among the 24 individuals I have selected from the Hofmeister group there is only one Nobel laureate (Otto Loewi, Physiology or Medicine), the numbers alone support Krebs's claim (note 7) that a chemist or a medical scientist who had worked with a previous winner was more likely to be a winner himself. A closer examination of the later successes of Fischer's more eminent progeny, however, shows little correlation between the award of Nobel prizes and the work they did in his laboratory. At best, it confirms the received opinion that eminent leaders in fashionable fields of science have attracted many talented young people. From the biographical sketches that follow it will be evident, I believe, that the men whose later efforts were most directly related to the work they did in Fischer's laboratory did not receive Nobel prizes. This is not to suggest that none of them deserved such public accolades, but this question involves the manner in which Nobel prize winners have been selected and will not be considered here.

While Fischer was still in Baeyer's Munich institute, one of his first predoctoral research students was Ludwig Knorr (1859–1921), whose dissertation dealt with an analogue of phenylhydrazine. Upon Fischer's appointment in Erlangen, Knorr accompanied him there and shortly afterward (1883) the study of the reaction of phenylhydrazine with ethyl acetoacetate led him to discover a pyrazole derivative that proved to be pharmacologically effective as a febrifuge. Fischer allowed Knorr to obtain a patent, and the manufacture of this product (*Antipyrine*) represented the entry of the Höchst dyeworks into pharmaceutical chemistry.[106] Af-

ter a brief stay with Fischer in Würzburg, Knorr became a full professor at Jena, where he directed the work of a sizable research group; several of his doctoral students joined Fischer as research assistants. Knorr's outstanding studies on pyrazoles and on the keto-enol tautomerism in substances related to ethyl acetoacetate stem directly from his association with Fischer. In addition, Knorr conducted a sustained program of research on alkaloids related to morphine. Fischer's liberality in encouraging Knorr to continue independent research along lines Fischer had initiated was not evident in relation to most of the other former junior members of his group. It is also noteworthy that after Knorr the men who achieved distinction as chemists were not associated with Fischer until after about 1899.

Among these was Otto Diels (1876–1954), son of the noted classical philologist in Berlin. For his Ph.D. dissertation he worked on cyanuric compounds and while an assistant in Fischer's institute he discovered carbon suboxide. As Professor of Chemistry at Kiel, Diels made important contributions to the elucidation of the structure of the sterol nucleus and, with his student Kurt Alder (1902–1958), developed the method of diene synthesis, for which both were awarded the Nobel Prize in Chemistry.[107]

The three other future Nobel prize winners in chemistry (Windaus, Hans Fischer, Pregl) stayed in Emil Fischer's laboratory only briefly. Adolf Windaus (1876–1959) received his Ph.D. in 1899 for work on digitalis alkaloids with Heinrich Kiliani, Professor of Medical Chemistry at Freiburg in Breisgau. After a short time with Fischer he returned to Kiliani who advised him to enter the sterol field. Among Windaus's many distinguished contributions, of special importance was his demonstration (with Alfred Hess) that a vitamin D can be produced by irradiation of yeast ergosterol with ultraviolet light. At Göttingen, where Windaus was Professor of Chemistry for almost 30 years, he led an

outstanding research group.[108] The second, Hans Fischer (1881–1945), had obtained both a Ph.D. in chemistry and an M.D. before his brief association in 1909 with Emil Fischer. On the advice of the noted Munich clinician Friedrich von Müller, who had concluded that bile pigments arise from hemoglobin, Hans Fischer entered a field opened in the previous century by the physiological chemists Felix Hoppe-Seyler and Marceli Nencki. His remarkable achievements over a 20-year period reached their peak in the synthesis of hemin, bilirubin and many porphyrins, thus establishing their chemical structure and paving the way for the later study of their metabolic formation and interconversion. After appointments as Professor of Medical Chemistry at Innsbruck and Vienna, in 1921 Hans Fischer became Professor of Organic Chemistry at the Munich *Technische Hochschule*.[109] The third, Fritz Pregl (1869–1930), was an Austrian physician who entered physiological chemistry at the turn of the century, and in 1904 spent a few months in Fischer's institute, where he was turned over to Abderhalden for training in the ester method of protein analysis. Upon his return to his native Graz, Pregl became an assistant in the medical-chemical laboratory, and in 1910 was appointed Professor of Medical Chemistry there. Pregl made his lifework the improvement of the available methods for the quantitative elemental analysis of organic compounds, and by 1917 he had devised new apparatus and techniques for the analysis of 2–3 milligram samples. The significance of this technical advance cannot be overestimated, for at a time when elemental analysis was still indispensable for the determination of organic-chemical structure, Pregl's microanalytical methods made it possible to analyze natural materials available to chemists in only small amounts.[110]

Next, mention may be made briefly of several former German associates of Fischer who did not win Nobel prizes but made important chemical contributions in fields un-related to Fischer's main research interests. In alphabetical order, they were: Franz Fischer (1877–1947) who became head of the Kaiser-Wilhelm Institute for Coal Research (organized by Emil Fischer) and who is best known for his work with Hans Tropsch on the artificial synthesis of benzene by high-pressure hydrogenation; Fischer's son Hermann O. L. Fischer (1888–1960) who did his doctoral work with Knorr and, after serving as one of his father's research assistants, made decisive contributions to the determination of the structure of quinic and shikimic acids and to the synthesis of biologically-important derivatives of glyceraldehyde; Carl Harries (1866–1923) whose studies on the ozonization of organic compounds and on rubber won him wide acclaim; Hermann Leuchs (1879–1945) who, after his work with Fischer on amino acids and peptides, discovered the N-carboxy amino acid anhydrides (which later attracted much attention for the synthesis of polypeptides), but whose main subsequent activity was in other fields, notably the strychnine alkaloids; Otto Ruff (1871–1939), who began as a pharmacist, then worked with Emil Fischer on sugars, and after 1903 played a leading role (comparable to that of the Nobel prize winner Henri Moissan) in the study of fluorine compounds; and Helmuth Scheibler (1882–1966) who, after his doctoral work with Fischer on peptides, turned to other organic-chemical problems, especially compounds containing divalent carbon, a subject that later became the important field of carbene chemistry.[111] To this group may be added Karl Spiro who, as was noted previously in this essay, began as an organic chemist with Fischer but, under the influence of Hofmeister, then worked on the physical chemistry of proteins and on other biochemical problems.

The two winners of Nobel prizes in physiology or medicine (Landsteiner, Warburg) were very different men. Karl Landsteiner (1868–1943) received his M.D. (Vienna) in 1891, and spent the following three years in

several organic-chemical laboratories. In addition to a year (1892) with Fischer, he also worked with Eugen Bamberger (Munich) and Arthur Hantzsch (Zurich). Landsteiner's remarkable achievements from 1897 onwards began with his discovery of human blood groups; his subsequent systematic work on the specificity of serological reactions laid the foundations of modern immunology. At the Rockefeller Institute for Medical Research, where he worked after 1922, he led a small group of able investigators, among them Alexander Wiener (1907–1976) and Philip Levine (b. 1900), with whom he discovered the rhesus (Rh) factor in human blood. Landsteiner was an unassuming person of broad culture and considerable chemical insight.[112]

Otto Warburg (1883–1970) completed his chemical studies in 1906 with Fischer; his Berlin dissertation dealt with the synthesis of several peptides by the halogenacyl halide method. An ambitious young man, with his sights set on more rewarding fields of endeavor (including the cancer problem), Warburg at once left organic chemistry and turned to cell physiology, apparently influenced by the writings of Jacques Loeb (1859–1924). Warburg's experimental work (on the respiration of fertilized sea urchin eggs) was conducted largely at the Naples biological experiment station during the years when he was studying medicine in Heidelberg. Three years after receiving his M.D. in 1911, Warburg became head of a laboratory of the Kaiser-Wilhelm Society; as Vice-President of the Society, Fischer was responsible for this appointment. Upon the outbreak of the First World War, Warburg at once joined a cavalry regiment, in which he served until the Armistice. Warburg later (1966) spoke enthusiastically about his war service: "I learned to handle people; I learned to obey and to command." During the 1920s he resumed his studies on cellular respiration, with special reference to oxidation and glycolysis in tumor cells. In connection with this work he devised new or improved experimental

methods in manometry and the use of tissue slices. He concluded that anaerobic glycolysis plays a primary role in the causation of cancer, a view he continued to reiterate into the 1960s, despite extensive evidence to the contrary. On the basis of experiments with model systems, Warburg insisted that the primary process in cellular respiration is the activation of protoplasmic iron, and he scornfully dismissed the work of Heinrich Wieland, Thorsten Thunberg and David Keilin showing that dehydrogenases and cytochromes play important roles in biological oxidations. Warburg received his Nobel prize for a brilliant spectrophotometric study of what he called the *Atmungsferment*. His greatest achievements came during the 1930s when he discovered the first of the flavoproteins, when he showed that the action of the dehydrogenases involves the participation of a nicotinamide-containing substance related to cozymase, and when his assistants Negelein and Wulff reported the first clear-cut demonstration of a coupling between oxidation and phosphorylation. In his polemics about the cancer problem and cellular respiration, as well as about photosynthesis, Warburg exhibited exceptional arrogance. His laboratory was run in semi-military fashion, and discipline was enforced by his personal servant Jacob Heiss. Warburg preferred to employ as his research assistants men who had been trained in technical schools rather than ambitious young scientists because "they never troubled him with requests for testimonials and for support in obtaining better posts." Although more generous than Fischer in allowing the names of these men (Walter Christian, Fritz Kubowitz, Erwin Negelein) to appear as authors of important papers from his institute, at the end of the Second World War Warburg abruptly dismissed them.[113]

I have dwelt at somewhat greater length on the career and personality of Otto Warburg not only because his work during the 1930s represents a peak of biochemical achievement in this century but also because

in later life he repeatedly stressed the importance of his association with Fischer. Although Warburg's claims for the special significance of the work he did in Fischer's laboratory either for protein chemistry or in his own later successes can be described most charitably as exaggerations, there can be little doubt that Warburg adopted much of Fischer's style in his conduct toward his collaborators.

The brief accounts given thus far of the later scientific activity of the more notable German or Austrian chemists or medical scientists who had worked in Fischer's successive laboratories suggest that, except for Knorr, most of them did not follow in Fischer's scientific footsteps. Four of those who all worked with him after 1900 did; they were Emil Abderhalden, Max Bergmann, Karl Freudenberg, Burckhardt Helferich and (from Austria-Hungary) Géza Zemplén.

Emil Abderhalden (1877–1950) was Fischer's faithful disciple, but the soundness of Fischer's assessment (see note 92) must be questioned in the light of the uncertainty of much of Abderhalden's work both as a member of Fischer's group and as an independent investigator later. Abderhalden became Professor of Physiology at the Berlin Veterinary School in 1908 and at Halle in 1911. He remained in Halle until 1945 when he was forcibly removed to the west by American forces before they were obliged to vacate the city under the interallied agreement dividing prewar Germany into four zones of occupation. Abderhalden ended his days in his native Switzerland. He was a man of inexhaustible energy and his skill as a scientific entrepreneur cannot be questioned; his output of scientific papers was enormous, and many of them dealt with proteins and peptides. He followed Fischer along the tracks that proved to be dead ends, notably in the continued use of the halogenacyl halide method of peptide synthesis and his espousal of Fischer's suggestion that diketopiperazines may be structural elements of

proteins. Abderhalden's claim for the existence of the *Abwehrfermente* (protective enzymes), elicited upon the parenteral administration to human subjects of foreign proteins, and his advocacy for at least 35 years of this supposed phenomenon as a test for pregnancy or cancer, can be described most generously as an example of sustained self-delusion. He also published many papers on other biochemical subjects, among them protein metabolism, vitamins and hormones.[114]

The scientific stature of Max Bergmann (1886–1944) was rather different. As Fischer's chief research assistant during the First World War, he worked on amino acids, depsides, carbohydrates and glycerides. Two years after Fischer's death Bergmann became Director of the newly-established Kaiser-Wilhelm Institute for Leather Research in Dresden. There, in addition to his service to the leather industry, he conducted an active research program that included distinguished work on carbohydrates, with special reference to unsaturated sugars (for example, glucal) and the polysaccharides cellulose and chitin, as well as on amino acids and peptides. For several years Bergmann, like Abderhalden, accepted the diketopiperazine theory of protein structure, and published a series of papers on unsaturated diketopiperazines. As was noted previously in this essay, in 1932 he and Leonidas Zervas reported the invention of the carbobenzoxy method of peptide synthesis; this advance marked the beginning of a new era in this field. In the following year Bergmann was forced by the Nazis to leave Germany and he moved to the Rockefeller Institute for Medical Research. It was my good fortune to be associated with him in New York from 1934 until his untimely death ten years later. There were two main lines of research. One involved the use of the newly-available peptides for the study of the specificity of proteolytic enzymes; my discovery of the first synthetic peptide substrates for pepsin and

other well-defined proteinases provided strong evidence for the peptide theory of protein structure at a time when the theory was under serious challenge. The other main line, actively pursued by Bergmann himself, was the development of new methods for the amino acid analysis of proteins. With Carl Niemann (1908–1964) he advanced the hypothesis that each kind of amino acid unit recurs at a regular periodic interval in the polypeptide chain of a protein; this excursion into numerology was based on inadequate analytical data and the Bergmann-Niemann periodicity hypothesis was soon shown to be invalid. Except for the interruption by work done in connection with the Second World War, the research on the amino acid composition and sequence of proteins continued at the Rockefeller Institute by Bergmann's associates William Howard Stein (1911–1980) and Stanford Moore (1913–1982) who shared the 1972 Nobel Prize in Chemistry for their achievements in this field.[115]

Carl Freudenberg (1886–1983) worked with Fischer between 1909 and 1914 on depsides and tannins. After the First World War he became Professor of Chemistry at Heidelberg, where over a period of 30 years he conducted fruitful research on the chemistry of carbohydrates and of lignins as well as in the field of stereochemistry, including the mechanism of the Walden inversion. Burckhardt Helferich (1887–1982), also a doctoral student and assistant with Fischer, worked in Berlin on the synthesis of glycosides. After the war he was successively Professor of Chemistry at Greifswald and Leipzig, but in 1945 he was removed to the west from the latter city by the American army; two years later he was appointed professor at Bonn. Helferich's main scientific achievements were in the synthesis of oligosaccharides, through the introduction of the triphenylmethyl (trityl) group for this purpose, and in the systematic study of the specificity of the enzymes that hydrolyze

glycosides. Géza Zemplén (1883–1956) received his Ph.D. in chemistry at Budapest in 1904 and three years later joined Fischer's group. Initially Zemplén worked on amino acids but toward the end of his stay in Berlin he was directed into the field of carbohydrate chemistry. He continued in this field afterward and made many outstanding contributions to the synthesis of oligosaccharides and of other naturally-occurring glycosides. As Professor of Organic Chemistry at the Technical University in Budapest, Zemplén played a leading role in the development of organic chemistry in post-war Hungary.[116]

The two dozen more renowned former members of the Fischer group also include one Frenchman and four Americans. Ernest Fourneau (1872–1949) had been a student at the great school of pharmacy in Paris before spending three years (1900–1902) in several German laboratories of organic chemistry. During his brief association with Fischer, he worked on derivatives of glycine; their joint paper in 1901 marked Fischer's entry into the peptide field (see note 14). After several years in the research laboratory of the Poulenc chemical company, in 1911 he joined the Pasteur Institute, where he conducted a sustained and fruitful search for effective new pharmaceutical agents. Among his many significant contributions were the preparation of the local anesthetic Stovaine and the demonstration that the active component of Gerhard Domagk's Prontosil is sulfanilamide. It would seem, therefore, that Fischer's interest in devising patentable drugs such as Veronal was a more important factor in Fourneau's later efforts than the work on peptides.[117]

The first of the notable Americans to work in Fischer's laboratory was Phoebus Aaron Theodore Levene (1869–1940). He received his M.D. in St. Petersburg in 1891 and, after several years of private medical practice in New York, entered biochemical research. During a visit to Europe in 1901 Levene spent a summer in Fischer's institute, where

he was assigned the task of analyzing gelatin by the ester method. In 1905 Levene was appointed to the staff of the newly-created Rockefeller Institute for Medical Research, and worked there until the end of his life on an extraordinary variety of biochemical problems. Chief among them was the constitution of the nucleic acids, a field that Fischer attempted to enter when he gave up hope of making a synthetic protein. Among Levene's publications (about 700) there were many papers dealing with proteins, and even before 1910 he did not hesitate to invade Fischer's territory by isolating peptides from partial hydrolysates of proteins. There were also experimental papers on the chemistry of phosphatides, cerebrosides and sugars, as well as on stereochemistry and on miscellaneous other topics. It was in the nucleic acid field, however, that Levene had the greatest impact, especially through the efforts around 1910 of his associate Walter Abraham Jacobs (1883–1967) who established that yeast nucleic acid is composed of ribonucleotides. Jacobs had received his Ph.D. in 1907 for work in Fischer's institute on the resolution of several amino acids. Five years later he became an independent investigator at the Rockefeller Institute, where he remained the rest of his life. During the First World War Jacobs's main activity was in the field of chemotherapy, and he made a major contribution through his discovery of Tryparsamide, effective in the treatment of African sleeping sickness. After the war he turned to the study of alkaloids, showed that many of those used in the treatment of heart disease were sterol derivatives, and later elucidated the complex structure of the ergot alkaloids. A modest person of exceptional chemical insight, Jacobs had an outstanding group of junior associates, among them Michael Heidelberger (b. 1888), Robert Cooley Elderfield (1904–1979) and Lyman Creighton Craig (1906–1974).

Another distinguished member of the Rockefeller Institute who worked in Fischer's Laboratory was Donald Dexter Van Slyke (1883–1971). After his Ph.D. (1907) in organic chemistry with Moses Gomberg at Michigan, Van Slyke joined Levene, with whom he worked on the amino acid composition of casein hydrolysates. On Levene's recommendation, Fischer accepted Van Slyke as a guest; during his brief stay (1910) in Berlin Van Slyke studied the properties of pyrrole carboxylic acid. His true genius became evident during 1911–1913 in his invention of a gasometric method for the determination of amino-nitrogen, and the use of this method to demonstrate (with Gustave Meyer) that proteins are cleaved completely to amino acids in the mammalian digestive tract and that amino acids disappear from the blood as it passes through the tissues; this marked the final burial of the peptone theory of protein synthesis. In 1914 Van Slyke became the chemist of the newly-opened hospital of the Rockefeller Institute; he worked there until 1949, and ended his days at the Brookhaven National Laboratory. It is probably fair to say that through his many contributions to quantitative clinical chemistry Van Slyke influenced medical practice to a greater degree than any other biochemist of this century. He remained a chemist to the end; for many years he worked on the structure of a new amino acid he had isolated from gelatin, and eventually showed it to be delta-hydroxylysine.

The fourth American visitor to Fischer's Berlin institute whom I have included in the list of those who later made significant contributions to the chemical or medical sciences, and the only one not associated with the Rockefeller Institute, was the pathologist Harry Gideon Wells (1875–1943). In accordance with Fischer's policy of turning post-M.D. guests over to Abderhalden for training in the ester method, upon his arrival in 1904 Wells was assigned keratin for analysis. In addition to his many later contributions to pathology, of special biochemical significance was his demonstration of the immu-

nological differences among the crystalline seed proteins provided by Thomas Burr Osborne (1859–1929).[118]

These biographical notes about the more notable former members of the Fischer group indicate the complexity of the problem of assessing the role that direct association with a famous leader has played in the later work of his successful progeny. In the case of the few who followed in Fischer's scientific footsteps after an extended stay in his laboratory, a positive influence is unmistakable. It is more difficult, however, to estimate the extent to which membership in his research group, especially when relatively brief, was reflected in the subsequent scientific output of the others. Indeed, it is conceivable that, whatever respect they may have had for Fischer's chemical genius, some of those who achieved later distinction found the tasks he assigned to them uninteresting. Obviously, the mere designation as a *Fischer-Schüler* and a favorable recommendation from him could be decisive in a person's professional advancement, but this says little about that person's choice of problems for independent research and the manner in which he tackled them.

I turn next to the members of the Hofmeister group whose later achievements are noteworthy, and will consider these men in three categories: those who continued to work in the biochemical sciences, those who specialized in other scientific disciplines (botany, physiology, pharmacology), and those who became clinical investigators.

Especially outstanding among the biochemists was Gustav Embden (1874–1933) who received his M.D. in Strassburg in 1899 and during the succeeding four years largely worked in Hofmeister's institute. There he investigated several biochemical problems before choosing for his lifework the study of intermediate metabolism. In 1904 he moved to a hospital laboratory in Frankfurt-am-Main; ten years later he was appointed Professor of Vegetative Physiology at the newly-created university in that city, and remained there until his death at a time when he was subjected to harassment by Nazi students. Embden was a pioneer in the use of perfusion techniques for the study of chemical changes in mammalian organs, and applied these methods fruitfully to the metabolic transformation of amino acids, fatty acids and sugars. During the 1920s his work on carbohydrate metabolism in muscle complemented that of the Nobel prize winner Otto Meyerhof (1884–1951). The high point of Embden's efforts in this field came in the final year of his life. He concluded that fructose-1,6-diphosphate is cleaved into glyceraldehyde-3-phosphate and dihydroxyacetone phosphate, and proposed a scheme for the conversion of glucose to lactic acid in muscle; this scheme was confirmed by Meyerhof in succeeding years. The establishment during the 1930s of the so-called Embden-Meyerhof pathway of anaerobic glycolysis represents one of the great successes of modern biochemistry.[119]

Among Embden's contemporaries at Strassburg was Franz Knoop (1875–1946).[70] He obtained his M.D. in 1900 at Freiburg, and moved to Hofmeister's institute, where he performed the experiments which led him to propose that the metabolic breakdown of fatty acids involves the removal of 2-carbon units through oxidation at the β-carbon. Knoop then returned to Freiburg where he later became Professor of Physiological Chemistry and after 1927 he held the same appointment in Tübingen. At both these universities he did important work on the metabolism of amino acids and of pyruvate; the aerobic oxidation of the latter metabolite was the subject of lively interest during 1920–1935. In particular, serious attention was given to a cyclic pathway via four-carbon dicarboxylic acids, based largely on the results of Knoop and of Thunberg, but this scheme had to be modified when Knoop and his associate Carl Martius showed in 1936 that citric acid also is an intermediate in the

aerobic oxidation of pyruvate. The solution of the problem came in the following year through the decisive experiments of Hans Krebs to demonstrate the operation of what has come to be known as the Krebs citric acid cycle.

In addition to Embden and Knoop, two other junior members of the Hofmeister group, Ernst Josef Friedmann (1877–1956) and Jacob Karol Parnas (1884–1949) later made outstanding contributions to the study of intermediate metabolism. Friedmann received both a Ph.D. (1902) and a M.D. (1905) for work he did at Strassburg. In addition to his achievement in establishing the structure of cystine, he conducted important studies on its metabolism in animals. In 1907 he returned to his native Berlin, where he became head of the chemistry laboratory in the medical clinic of the Charité hospital; there, his research included a distinguished series of investigations on the metabolic formation of ketone bodies. In 1930 he left Germany and went to Cambridge, England where he remained the rest of his life.

Parnas was born in Poland (then under Russian rule), studied organic chemistry in Germany, and obtained his Ph.D. (1908) in Munich for work done with Richard Willstätter. He then went to Hofmeister's institute, where he worked on cephalin and aldehyde mutase before embarking on a lifelong investigation of carbohydrate metabolism in muscle. Parnas remained in Strassburg until 1916, when he returned to Poland; from 1920 to 1941 he was Professor of Physiological Chemistry in Lwów. There he established an important school, whose achievements included the elucidation of the phenomenon of ammonia formation during muscular contraction and the discovery of the enzymatic phosphorolysis of muscle glycogen. The process of anaerobic glycolysis in muscle is often termed the Embden-Meyerhof-Parnas pathway.[120]

Hofmeister's personal research in Prague dealt largely with proteins, and it is not sur-prising that several of his more notable former associates continued in this field. Wolfgang Pauli (1869–1955) worked for his M.D. dissertation (1892) in Hofmeister's laboratory; after a few years of clinical service in Vienna, Pauli turned to the study of the physical chemistry of proteins. He was among the first to follow up the observations of William Bate Hardy (1864–1934) on the movement of proteins in an electric field. During the course of his extensive studies on the electrophoresis of proteins, Pauli devised some of the early apparatus in the field. Through his many writings, especially several books, he became one of the leading advocates of the colloid-chemical approach to the study of proteins. In 1922 Pauli was appointed Professor of Medical Colloid Chemistry at Vienna, but was obliged to leave after the Nazis invaded Austria.

Another Austrian, Otto von Fürth (1867–1938), came to Hofmeister after his M.D. (1894) in Vienna, and accompanied him to Strassburg. During his association with Hofmeister, Fürth began studies on muscle proteins, a subject he continued to pursue in later years. He also worked on the adrenal hormone he named *Suprarenin*, which was marketed under that name by Höchst; in this field he was in competition with the American investigators Takamine and Aldrich who had crystallized the hormone and named it *Adrenaline*. Fürth's interest in this substance stemmed from his earlier work with Hofmeister on the chemical reactions of the tyrosine units of proteins; later he also studied the enzyme tyrosinase and the melanins. Fürth returned to Vienna in 1905 and eventually became Professor of Medical Chemistry there.[121]

As was noted in a previous section of this essay, Hofmeister's most valuable junior colleague in Strassburg was Karl Spiro, who made significant contributions to the study of the physical chemistry of proteins.[68] In his later professorship of physiological chemistry in Basel (1921–1932) Spiro fol-

lowed Hofmeister's example in encouraging the independent efforts of his associates. Mention has also been made before of Lawrence J. Henderson's stay in Strassburg and of his relationship to Hofmeister and Spiro.[72] Henderson later became Professor of Biological Chemistry at Harvard. Although not an enthusiastic experimenter, he performed outstanding studies on acid-base balance in biological fluids and he wrote several books (*The Fitness of the Environment, The Order of Nature, Blood: A Study in General Physiology*) that greatly influenced contemporary biological thought. Still another member of the Hofmeister group who later achieved considerable distinction was Ernst Peter Pick (1872–1960) who came to Strassburg after his M.D. (1896) in Prague. During the succeeding three years he used the salting-out method in efforts to separate the peptide cleavage products of proteins. Pick then went to the Austrian Serum Institute in Vienna; there, with Friedrich Obermayer (1861–1925), he made the important discovery that chemical modification of a protein can produce antigens which elicit the formation of antibodies specific for the modified protein. In 1911 Pick joined the Vienna pharmacologist Hans Horst Meyer, and succeeded him as Professor of Pharmacology in 1924. Pick was forced to leave Vienna in 1938 and came to the United States where he continued pharmacological work, largely at the Merck Institute for Therapeutic Research.[122]

Among the more notable biochemical progeny of Hofmeister's Strassburg institute must also be included Wilhelm Stepp (1882–1964) and Henry Stanley Raper (1882–1951). Stepp went to Strassburg after his M.D. (1907) in Munich. At that time Hofmeister was increasingly drawn to the study of what he called "accessory nutrients," and Stepp's demonstration in 1909 of the nutritional requirement for a fat-soluble factor was one of the important events at the beginning of the vitamin era. Stepp later became Professor of Medicine, first at Jena, then in Munich,

where he conducted an active program of research in the vitamin field. Raper began in 1902 as an organic chemist with Julius Berend Cohen (1859–1935) in Leeds and then joined John Beresford Leathes (1864–1956) in studies on fat metabolism at the Lister Institute. It should be noted that during the first decade of this century, the Lister Institute was the principal center of British biochemical research; in addition to Leathes, there were Harden and Young, Charles James Martin (1866–1955) and Henry Drysdale Dakin (1880–1952). During his association with Leathes, Raper was encouraged to spend a year (1905–1906) in Strassburg, and worked there on the separation of the enzymic cleavage products of proteins. In 1910 Raper obtained a D.Sc. at Leeds and qualified for medical practice; in 1923 he became Professor of Physiology at Manchester. He made significant contributions to the study of fat metabolism along the lines initiated by Knoop and to the elucidation of the role of tyrosinase in the formation of melanins. Friedrich Czapek (1868–1921) worked in Hofmeister's Prague laboratory during the course of his medical studies. After receiving the M.D. degree in 1892, Czapek began studies in plant physiology with Wilhelm Pfeffer (1845–1920) in Leipzig, and in 1894 obtained his Ph.D. in Vienna. Czapek later became Professor of Botany in Prague and shortly before his death had been selected to be Pfeffer's successor. Czapek's many contributions to plant biochemistry and physiology, as well as his book *Die Biochemie der Pflanzen* (dedicated to Hofmeister and Pfeffer), gave evidence of his wide-ranging biochemical interests.[123]

In addition to Pick, four other former Hofmeister associates became noted pharmacologists. The most famous of them was Otto Loewi;[74] the others were Julius Pohl (1861–1942), Alexander Ellinger (1870–1923) and Siegfried Loewe (1884–1963). Pohl had been a student and assistant of Hofmeister before succeeding him as Pro-

fessor of Pharmacology in Prague, where he did important work on the metabolism of alcohols, the action of bromoacetic acid on muscle, and the toxicity of chloroform; in these investigations Pohl drew conclusions that were accepted only many years later. Ellinger obtained his Ph.D. (1892) in organic chemistry and then pursued medical studies in Strassburg, where he worked with Spiro on the anticoagulant action of peptones. In 1897 Ellinger went to Max Jaffé (1841–1911), the noted biochemist who was Professor of Pharmacology at Königsberg, where Ellinger obtained his M.D. degree. He succeeded Jaffé but in 1914 moved to the newly-created university in Frankfurt. Before his untimely death, Ellinger conducted outstanding biochemical research on the chemistry and metabolism of several amino acids, notably tryptophan, and on various pharmacological problems; like other noted former members of the Hofmeister group, he encouraged the independent efforts of his junior associates. Loewe worked with Hofmeister for his M.D. thesis (1908) on the cleavage of proteins by pepsin. Shortly afterward Loewe began research in pharmacology with Wolfgang Heubner (1877–1957) in Göttingen, and remained there until 1921 when he was appointed Professor of Pharmacology in Dorpat (Tartu). Loewe moved to Mannheim in 1928, but was forced to leave Germany five years later; during the remainder of his life he worked at Cornell Medical College and the University of Utah. Loewe's distinguished contributions to pharmacology included studies on sex hormones and the active ingredients of hashish.[124]

The association of the physiologist Albrecht Bethe (1872–1954) with the Hofmeister group was in one sense brief, through his work in 1905 on the staining of tissues, and in another sense lengthy, because of his leading role in bringing together the younger members of various departments in the Strassburg medical faculty. Bethe received his M.D. (1898) in Strassburg for a study on

the histology of nerve cells, and in succeeding years won renown for his investigations on nerve conduction, the permeability of tissue membranes and the periodicity of physiological processes. He left Strassburg in 1911 to go to Kiel, and four years later became Professor of Physiology at Frankfurt, where he joined his former Strassburg colleagues Embden and Ellinger.[125]

To conclude this set of sketches, mention must be made of the more notable former Hofmeister associates who made their reputation through distinguished contributions to clinical investigation. The first of these was Friedrich Kraus (1858–1936) who became an assistant in Hofmeister's Prague institute after receiving his M.D. there in 1882. After serving as Professor of Medicine in Graz (1894–1902), Kraus was appointed to the prestigious chair of medicine at the Charité Hospital in Berlin, where he established a productive school; his studies dealt largely with metabolic and cardiovascular disorders. In 1927 Kraus was succeeded at the Charité by another former Hofmeister student, Gustav von Bergmann (1878–1955), who had received his M.D. (1903) in Strassburg for work on the metabolic conversion of cystine to taurine. Bergmann then joined Kraus and, after holding posts in Hamburg and Marburg, returned to Berlin, where he continued to make significant contributions to the study of metabolic dysfunctions. Still another Hofmeister student in Prague was Adalbert Czerny (1863–1941); he received his M.D. in 1888 and later was successively Professor of Pediatrics in Breslau, Strassburg and (after 1913) in Berlin. Czerny conducted notable investigations on the clinical aspects of digestion and metabolism in children.[126]

To these distinguished clinicians must be added Adolf Magnus-Levy (1865–1955), Léon Blum (1878–1930), Hans Eppinger (1879–1946) and Ernst Freudenberg (1884–1967). Before coming to Strassburg, Magnus-Levy had obtained his M.D. (1890) in Leipzig and his Ph.D. in chemistry (1893) in Erlan-

gen, and in 1895 had discovered the relation of the thyroid to the respiratory exchange (basal metabolic rate). In Bernhard Naunyn's Strassburg clinic, Magnus-Levy also elucidated the cause of diabetic acidosis and found time to work in Hofmeister's laboratory on the crystallization of the Bence-Jones protein by the salting-out method. In 1901 he moved to Berlin, where he had a private medical practice and conducted research on various clinical subjects at the Charité hospital. After having been arrested by the Nazis, Magnus-Levy succeeded in coming to the United States in 1940. Blum was one of the several Frenchmen whom Hofmeister encouraged during the German occupation of Alsace-Lorraine. His M.D. dissertation (1901) dealt with the nutritional quality of albumoses and he also worked on the metabolism of cystine. As one of Naunyn's assistants Blum made notable contributions to the study of diabetes and other metabolic disorders; upon the reversion of Strasbourg to French rule in 1918, Blum became Professor of Medicine there. Eppinger, a student of Friedrich Kraus in Graz, received his M.D. there in 1903, and then worked in Hofmeister's laboratory on the metabolic formation of urea and allantoin. After several years as an associate of the noted clinician Carl von Noorden in Vienna, Eppinger became Professor of Medicine in Freiburg, but returned to Vienna in 1933 to head the First University Medical Clinic. His research interests were very broad, and he made significant contributions to the study of numerous clinical problems. Freudenberg spent a year (1912–1913) with Hofmeister after his M.D. in Munich, and worked on fat metabolism. After military service in the First World War he became Professor of Pediatrics at Marburg, but was dismissed in 1933 and moved

to Basel where he held the same post until 1954. Freudenberg's principal research achievements were in the study of metabolic disorders in children.[127]

The assessment of Hofmeister's contribution to the success of his scientific progeny is fraught with as much uncertainty as in the case of the notable former members of the Fischer group. That there was considerable positive influence is indicated by the later research, as well as the testimony, of several Hofmeister people, but the contrary evidence offered by Lawrence J. Henderson cannot be disregarded. I believe, however, that both the numerical data in Table 2 and my qualitative estimates of the subsequent achievements of two dozen successful former members of each group support the conclusion that the educational contributions of Fischer and Hofmeister to the advancement of the biochemical sciences were more nearly equal than is implied by the disparity in the place accorded these two men in the history of the sciences. Moreover, the examination of their research groups suggests that selective genealogical tables offer little insight into the relation of the fame of a group leader to the later renown of his scientific progeny. For the fuller understanding of the development of the biochemical sciences, historians need to look more closely at productive research groups whose leaders received modest recognition for their personal research, and not only at individuals whose names are directly associated with great scientific advances.

Notes

1. J. B. Morrell, "The Chemist Breeders: The Research Schools of Liebig and Thomas Thomson," *Ambix* 19 (1972): 1–46. For an account of the relation of university research groups to the growth of German chemical industry see L. Burchardt, "Professionalisierung oder Berufskonstruktion? Das Beis-

piel des Chemikers im Wilhelminischen Deutschland," *Geschichte und Gesellschaft* 6 (1980): 326–348.

2. H. H. Eulner, *Die Entwicklung der medizinischen Spezialfächer an den Universitäten des deutschen Sprachgebietes* (Stuttgart 1970); for a brief history of the development of health care in Wilhelmine Germany see M. Stürzbecher, "Die medizinische Versorgung und die Entstehung der Gesundheitsfrage zu Beginn des 20. Jahrhunderts in Deutschland," in G. Mann and R. Winau (Eds.), *Medizin, Naturwissenschaft und Technik und das zweite Kaiserreich* (Göttingen 1977), 239–258.

3. A. Delaunay, *L'Institut Pasteur, des origines à aujourd'hui* (Paris 1962); H. Chick, M. Hume and M. Macfarlane, *War on Disease: A History of the Lister Institute* (London 1971); G. W. Corner, *A History of the Rockefeller Institute 1901–1953* (New York 1964); G. Wendel, *Die Kaiser-Wilhelm Gesellschaft 1911–1914* (Berlin 1975).

4. Of the many recent books and articles on the social organization of scientific research only a few can be cited: D. C. Pelz and F. M. Andrews, *Scientists in Organizations: Productive Climates for Research and Development* (New York 1966); S. R. Mikulinsky, M. G. Jarosevskij, G. Kröber and H. Steiner, *Wissenschaftliche Schulen* (Berlin 1977, 1979); F. M. Andrews (ed.), *Scientific Productivity* (Cambridge 1979); G. L. Geison, "Scientific Change, Emerging Specialties and Research Schools," *History of Science* 19 (1981): 20–40; T. Jagtenberg, *The Social Construction of Science* (Dordrecht 1983).

5. Much has been written on the reward system in science. For example, S. Cole and J. R. Cole, "Scientific Output and Recognition: A Study on the Reward System in Science," *American Sociological Review* 32 (1967): 377–390; R. K. Merton, "The Matthew Effect in Science," *Science* 59 (1968): 56–63; S. S. Blume and R. Sinclair, "Chemists at British Universities: A Study in the Reward System in Science," *American Sociological Review* 38 (1973): 126–138. Special attention has been given to the award of Nobel Prizes; see C. G. Bernhard, E. Crawford and P. Sörbom (Eds.), *Science Technology and Society in the Time of Alfred Nobel* (Oxford 1982), particularly the valuable papers by E. Crawford and R. M. Friedman (pp. 311–331) and by C. Salomon-Bayet (pp. 377–400). It should perhaps be noted here that if the leader of a closely-directed research group received most of the reward for success, he was also required to accept responsibility for any mistakes or falsifications in publications bearing his name.

6. For Morrell, see note 1. G. L. Geison, *Michael Foster and the Cambridge School of Physiology: The Scientific Enterprise in Late Victorian Society* (Princeton 1978).

7. H. A. Krebs, "The Making of a Scientist," *Nature* 215 (1967): 1441–1445. A critical study of the life, work and thought of Hans Adolf Krebs (1900–1981) is being prepared by my Yale colleague Professor Frederic L. Holmes, whose obituary notice for Krebs appeared in the Year Book of the American Philosophical Society (1982): 501–507.

8. For a brief history of the Society of German Scientists and Physicians see R. Bochalli, "Die Gesellschaft deutscher Naturforscher und Ärzte als Spiegelbild der Naturwissenschaften und der Medizin," *Naturwissenschaftliche Rundschau* 1 (1948): 275–278; unaccountably, he refers to 1902 Karlsbad session as the 75th meeting. Other articles dealing with special aspects of the history of the Society appeared in subsequent issues of *Naturwissenschaftliche Rundschau.*

9. See R. H. A. Plimmer, *The Chemical Constitution of the Proteins* (London 1908); H. B. Vickery and T. B. Osborne, "A Review of Hypotheses of the Structure of Proteins," *Physiological Reviews* 8 (1928): 393–446; F. Lieben, *Geschichte der Physiologischen Chemie* (Leipzig and Vienna 1935), 359–391; J. S. Fruton, *Molecules and Life* (New York 1972), 148–179; A. N. Shamin, *Istoria Khimii Belka* (Moscow 1977), 134–278; J. S. Fruton, "Early Theories of Protein Structure," *Annals of the New York Academy of Sciences* 325 (1979): 1–18.

10. F. Hofmeister, "Ueber den Bau des Eiweissmoleküls," *Naturwissenschaftliche Rundschau* 17 (1902): 529–533, 545–549. The text of the lecture was an adaptation for a general audience of Hofmeister's review article "Über Bau und Gruppierung der Eiweisskörper," *Ergebnisse der Physiologie* 1 (1902): 759–802. This journal was established by Leon Asher and Karl Spiro.

11. For a comprehensive account of the history of the biuret reaction see F. Kurzer, "Biuret and Related Compounds," *Chemical Reviews* 56 (1956): 95–197.

12. For an appreciation of the contributions of Theodor Curtius (1857–1928) see C. Freudenberg, "Theodor Curtius," *Chemische Berichte* 96 (1963): i–xxv.

13. E. Fischer, "Über die Hydrolyse der Proteinstoffe," *Chemiker-Zeitung* 26 (1902): 939–940.

14. E. Fischer and E. Fourneau, "Über einige Derivate des Glykocolls," *Berichte des deutschen chemischen Gesellschaft* 34 (1901): 2868–2877.

15. There have been numerous treatments of this subject before and after the famous article by R. K. Merton, "Singletons and Multiples in Scientific Discovery," *Proceedings of the American Philosophical Society* 105 (1961): 470–486. For example see H. U. Baumann, *Über Mehrfachentdeckungen* (Münster 1972); the Fischer-Hofmeister peptide theory of protein structure is listed on p. 66. One view of the priority in this case was offered by Hofmeister's former assistant Otto von Fürth in his obituary notice for Fischer in *Wiener klinische Wochenschrift* 32 (1919): 828–829: "In 1902, on the occasion of the Karlsbad meeting, Franz Hofmeister first formulated scientifically the assumption of an amide-like linkage of the individual amino acids within protein. E. Fischer was however the one who attacked the problem systematically."

16. Whether Fischer and Hofmeister actually met face-to-face at the Karlsbad session, or anywhere else, is uncertain. I have found no reference to such a personal meeting, nor have I found any evidence for an exchange of letters between them. None

are included in the extensive collection of Fischer's correspondence at the Bancroft Library in Berkeley; the only indications of a contact is through Hofmeister's Strassburg associate Spiro, who had obtained his Ph.D. in chemistry with Fischer (e.g., letter from Spiro to Fischer, 27 January 1901). I am greatly indebted to Miss Marie Byrne and her colleagues at the Bancroft Library for their generous assistance in my study of the Emil Fischer Collection. For a useful description of the collection see N. X. Jacobs, "The Emil Hermann Fischer Papers," *The Mendel Newsletter* No. 22 (1983): 1–10.

17. In 1910, Fischer was elevated to the rank of *wirklicher Geheimer Rat*, which required that he be addressed as *Exzellenz*.

18. The emergence of biochemistry as a major scientific discipline during the twentieth century, and the place of research on proteins in that development, have been treated in: J. S. Fruton, "The Emergence of Biochemistry," *Science* 192 (1976): 327–334; P. R. Srinivasan, J. S. Fruton and J. T. Edsall (Eds.), The *Origins of Modern Biochemistry: A Retrospect on Proteins* (New York 1979); R. E. Kohler, *From Medical Chemistry to Biochemistry: The Making of a Biomedical Discipline* (Cambridge 1982). For reviews of the last-named work see F. L. Holmes, *Nature* 300 (1982): 779–800 and L. G. Wilson, *Journal of the History of Medicine* 38 (1983): 462–464.

19. Adolf von Baeyer (1835–1917) played a decisive role in making German organic chemistry preeminent after 1870. In addition to Fischer, his students included Eduard Buchner, Theodor Curtius, Johannes Thiele and Richard Willstätter. See E. Fischer, in Adolf von Baeyer *Gesammelte Werke* (Braunschweig 1905), xxi–xxvii; H. Rupe, *Adolf von Baeyer als Lehrer und Forscher* (Stuttgart 1932); K. Schmorl, *Adolf von Baeyer* (Stuttgart 1952); R. Willstätter, *From My Life*, translated by L. S. Horning (New York, 1965), 109–153.

20. C. Harries, "Emil Fischers wissenschaftliche Arbeiten," *Naturwissenschaften* 17 (1919): 843–860.

21. An extensive bibliography of writings about Fischer may be found in J. C. Poggendorff, *Biographisch-literarisches Handwörterbuch zur Geschichte der exacten Naturwissenschaften* Vol. 7a Supplement (Berlin 1971), 204–207. Among the excellent general accounts of his scientific work are: C. Harries (note 20), M. O. Forster, "Emil Fischer Memorial Lecture," *Transactions of the Chemical Society* 117 (1920): 1157–1201; K. Hoesch, *Emil Fischer, sein Leben und sein Werk* (Berlin and Leipzig 1921); G. Hilgetag and P. Paul, "Zur wissenschaftlichen Leistung Emil Fischers," *Zeitschrift für Chemie* 10 (1970): 281–289.

22. E. Fischer, *Über Fluorescein und Phthalein-Orcin* (Bonn 1874). Most of his subsequent papers on dyes of that class were published in collaboration with his cousin Otto Fischer (1852–1932).

23. E. Fischer, "Ueber die Hydrazinverbindungen," Liebigs *Annalen der Chemie* 190 (1878): 67–183; 199 (1879): 281–332.

24. E. Fischer, *Aus Meinem Leben* (Berlin 1922), 77.

25. For accounts of Fischer's work on indoles see P. A. Roussel, "The Fischer Indole Synthesis," *Journal of Chemical Education* 30 (1953): 122–125 and B. Robinson, *The Fischer Indole Synthesis* (New York 1983). Among the many articles about Fischer's work on sugars especially noteworthy are: C. S. Hudson, "Emil Fischer's Discovery of the Configuration of Glucose," *Journal of Chemical Education* 18 (1941): 353–357; "Historical Aspects of Emil Fischer's Fundamental Conventions for Writing Stereo-formulas in a Plane," *Advances in Carbohydrate Chemistry* 3 (1948): 1–22; K. Freudenberg, Emil Fischer and his Contribution to Carbohydrate Chemistry," ibid. 21 (1966): 1–38.

26. E. Fischer, "Einfluss der Konfiguration auf die Wirkung der Enzyme I," *Berichte der deutschen chemischen Gesellschaft* 27 (1894): 2985–2993.

27. E. Fischer, "Synthesen in der Puringruppe," ibid. 32 (1899): 435–504. For Ludwig Medicus (1847–1915) see L. Reitzenstein, ibid, 48 (1915): 1744–1748.

28. Albrecht Kossel (1853–1927) was the most productive disciple of Felix Hoppe-Seyler, and became Professor of Physiology at Heidelberg. His chemical work between 1880 and 1895 on the material that Friedrich Miescher had named *nuclein* laid the groundwork for later research on nucleic acids. In addition to adenine and guanine, Kossel isolated thymine, which Fischer synthesized in 1901. After 1895 Kossel made important contributions to protein chemistry. He received the Nobel Prize in physiology or medicine for 1910. See S. Edlbacher, "Albrecht Kossel zum Gedächtnis," *Zeitschrift für physiologische Chemie* 177 (1928): 1–14 and M. E. Jones, "Albrecht Kossel, a Biographical Sketch," *Yale Journal of Biology and Medicine* 26 (1953): 80–97.

29. C. V. Ratnam, "Depsides: A Synthesis by Emil Fischer," *Journal of Chemical Education* 38 (1961): 93–94.

30. The format of all these volumes was established by Fischer himself, and he edited the first four: *Untersuchungen über Aminosäuren, Polypeptide und Proteine 1899–1906* (Berlin 1906); *Untersuchungen in der Puringruppe 1882–1906* (Berlin 1907); *Untersuchungen über Kohlenhydrate und Fermente 1884–1908* (Berlin 1909); *Untersuchungen über Depside und Gerbstoffe 1908–1919* (Berlin 1919). The fourth one was completed shortly before Fischer's death, and the final stages of its publication were supervised by Max Bergmann, who also edited the later volumes: *Untersuchungen über Kohlenhydrate und Fermente II 1908–1919* (Berlin 1922); *Untersuchungen über Aminosäuren, Polypeptide und Proteine II 1907–1919* (Berlin 1923); *Untersuchungen über Triphenylmethanfarbstoffe, Hydrazine und Indole* (Berlin 1924); *Untersuchungen aus Verschiedenen Gebieten* (Berlin 1924). The last contains scientific articles that did not appear in the earlier volumes as well as various lectures and obituary notices written by Fischer. Bergmann also arranged

for the publication of Fischer's autobiography (up to about 1900) written near the end of his life (see note 24).

31. A valuable study of Fischer's research group has been prepared by L. Läsker, "Characterische Besonderheiten der Schule von Emil Fischer," in Mikulinsky et al. (see note 4), Vol. 2, pp. 99–112.

32. Fischer's pharmaceutical patents, especially those for the barbiturate Veronal and for Sajodin (an iodine compound designed to release iodide slowly) were especially profitable. His relations to leaders of the German chemical industry were cordial, and very close in the case of Carl Duisberg (1861–1935), head of Friedrich Bayer and Co., Leverkusen. They had met in 1883 when Duisberg was a student in Baeyer's institute in Munich, and their extensive correspondence continued until Fischer's death. See C. Duisberg, "Emil Fischer und die Industrie," *Berichte der deutschen chemischen Gesellschaft* 52A (1919): 149–164. Fischer also had close connections to other chemical companies, especially those (such as C. F. Boehringer and Sons, Waldhof-Mannheim) where several of his former students or assistants had risen to executive positions.

33. From data in the archives of the Humboldt University, Läsker (note 31) estimated that around 1905 Fischer had about 10 coworkers; although not stated, presumably this number refers to paid research assistants. Ten years later, after the outbreak of the war, only two people (Max Bergmann, Charlotte Rund) occupied Fischer's *Privatlaboratorium*, and in the large student laboratory there were only 6 *Praktikanten*, 3 of whom were women. Earlier, Fischer did not encourage women to undertake work toward the Ph.D. in chemistry; see *Aus meinem Leben* (note 24), 192.

34. See A. Busch, *Die Geschichte der Privatdozenten* (Stuttgart 1959); "The Vicissitudes of the *Privatdozent*: Breakdown and Adaptation in the Recruitment of the German University Teacher," *Minerva* 1 (1963): 319–341. For an incisive account of the assistantship system in pre-World War II Germany, see K. D. Bock, *Strukturgeschichte der Assistentur* (Düsseldorf 1972). A valuable account of German student life has been prepared by K. H. Jarausch, *Students, Society and Politics in Imperial Germany* (Princeton 1982). For a detailed compilation of data on the changes in the composition and social origins of the faculties of German universities see C. von Ferber, *Die Entwicklung des Lehrkörpers der deutschen Universitäten und Hochschulen 1864–1954* (Göttingen 1956). From these sources it is clear why German scientists were largely drawn from the upper middle class, since the sons of titled families tended to enter military or civilian government service and, owing to the cost and uncertainty of the road to a university professorship, it was closed to sons of workers and small farmers.

35. M. Bergmann, "Emil Fischer," in *Das Buch der grossen Chemiker* (Berlin 1929, 1930), 2: 408–420; for the quotation see 415.

36. M. O. Forster (note 21), 1158.

37. J. B. Herrick, *Memories of Eighty Years* (Chicago 1949), 130–131.

38. F. Herneck, "Emil Fischer als Mensch und Forscher," *Zeitschrift für Chemie* 10 (1970): 41–48; for the quotation, see 45. For a history of the Berlin Chemical Institute, see K. Heinig, "Das Chemische Institut der Berliner Universität unter der Leitung von August Wilhelm Hofmann und Emil Fischer," *Forschen und Wirken: Festschrift zur 150-Jahr-Feier der Humboldt-Universität zu Berlin* (Berlin 1960), 1: 339–357. In his admirable account of the research group led by Justus von Liebig at Giessen, Morrell (see note 1) stressed Liebig's encouragement of self-reliance and independent thought. Some of his famous students, notably A. W. Hofmann, followed his example. Beginning with Adolf von Baeyer, however, a more dictatorial attitude became the prevailing norm in German university institutes of organic chemistry.

39. L. Lewin, "Eine toxikologische Erinnerung an Emil Fischer," *Naturwissenschaften* 7 (1919): 878–892.

40. R. Günther, ". . . Vertrauen auf die Weisheit einer Hohen Staatsregierung . . . Die Berufung des Nobelpreisträgers Emil Fischer," *Würzburg-Heute* 29 (March 1980): 21–22.

41. *Aus meinem Leben* (note 24), 126.

42. E. Trendelenburg, "Emil Fischer in seiner Betätigung für die deutsche Wissenschaftspflege," *Naturwissenschaften* 7 (1919): 873–876. See also G. Wendel (note 3).

43. Letter from Fischer to Abderhalden, 14 March 1912, Bancroft Library. It is difficult to surmise who particularly aroused Fischer's ire; possible candidates for this distinction are Phoebus A. Levene and Thomas B. Osborne.

44. See K. Schwabe, *Wissenschaft und Kriegsmoral* (Göttingen 1969), 22–23. For the full text of the *Aufruf* and a complete list of the signers, see H. Kellermann, *Der Krieg der Geister* (Dresden 1915), pp. 64–68. The other chemists on the list were von Baeyer, Karl Engler, Fritz Haber, Wilhelm Ostwald and Wilhelm Willstätter. The medical sciences were represented by Emil von Behring, Paul Ehrlich, Albert Neisser, Wilhelm Röngten, Max Rubner, Wilhelm Waldeyer and August von Wassermann. A notable omission is the name of Albrecht Kossel.

45. A. Weinberg, "Emil Fischers Tätigkeit während des Krieges," *Naturwissenschaften* 7 (1919): 868–873

46. For a perceptive account, based largely on the Fischer collection in the Bancroft Library, see G. D. Feldman, "A German Scientist between Illusion and Reality: Emil Fischer 1909–1919," in l Geiss and B. J. Wendt (Eds.), *Deutschland in der Weltpolitik des 19. und 20. Jahrhunderts* (Düsseldorf 1973), 341–362.

47. The published biographical material about Franz Hofmeister is much less extensive than that for Emil Fischer. The most important source is J. Pohl and K. Spiro, "Franz Hofmeister, sein Leben and Wirken," *Ergebnisse der Physiologie* 22 (1923): 1–50. Other articles, mostly obituary notices, will be mentioned later in this essay.

48. W. Koerting, *Die Deutsche Universität in Prag. Die*

letzten hundert Jahre ihrer Medizinischen Fakultät (Munich 1968). This work contains material published by Koerting in *Bayerisches Ärzteblatt* 22 (1967): 802–818, dealing with the Departments of Physiology, of Physiological and Medical Chemistry, and of Pharmacology.

49. Ewald Hering (1834–1918) is best known for his theories of vision and the fact that in 1870 he succeeded Jan Purkyně at Prague and in 1895 Carl Ludwig at Leipzig. See V. Kruta, *Dictionary of Scientific Biography* (New York 1972) 6: 299–301. Hering's article "Zur Theorie der Vorgänge in der lebendigen Substanz," *Lotos* 37 (1888): 35–70 may have stimulated Hofmeister's interest in intracellular metabolism. For Hugo Huppert (1834–1904) see R. von Zeynek, *Prager medizinische Wochenschrift* 29 (1904): 593–596.

50. For an account of the peptone theory of protein synthesis see J. S. Fruton, *Molecules and Life* (New York 1972), 431–432. By 1912 it was clear that amino acids, not peptones, are the metabolic precursors of blood proteins, and O. von Fürth wrote in his *Probleme der physiologischen und pathologischen Chemie* (Leipzig 1912), 1: 77: "There are few chapters in physiological chemistry that show more clearly the rapidity with which scientific ideas change than the doctrine of the albumoses and peptones. . . . How little of what I learned with great pains has importance today, and how many of the problems that the previous generation of physiologists fought about so passionately have lost for us any sense or significance."

51. A student of Felix Hoppe-Seyler, Oswald Schmiedeberg (1838–1921) was a leading figure in the establishment of pharmacology as an independent discipline in German medical faculties. Apart from his important pharmacological studies (for example, on muscarine), he made significant biochemical contributions in his work on the crystallization of seed globulins, the nature of glycoproteins, the metabolic oxidation of foreign organic substances and the biosynthesis of urea and of hippuric acid. See H. H. Meyer, "Schmiedebergs Werk," *Archiv für experimentelle Pathologie und Pharmakologie* 92 (1922): i–xxvii; J. Koch-Weser and P. J. Schachter, "Schmiedeberg in Strassburg 1872–1918: The Making of Modern Pharmacology," *Life Sciences* 22 (1978): 1361–1371.

52. A useful discussion of the Hofmeister series, and a biographical sketch, was published by J. L. Abernethy, "Franz Hofmeister: The Impact of his Life and Research on Chemistry," *Journal of Chemical Education* 44 (1967): 177–180. A brief biographical note about Camille Méhu (1835–1887) was prepared by E. V. McCollum, ibid. 33 (1956): 507. For the crystallization of egg albumin see F. Hofmeister, "Über die Darstellung von kristallisierten Eieralbumin und die Kristallisierbarkeit kolloider Stoffe," *Zeitschrift für physiologische Chemie* 14 (1889): 165–172.

53. A representative treatise during the first decade of this century was H. Freundlich, *Kapillarchemie* (Leipzig 1909).

54. J. Pohl, "Ueber die Oxydation des Methyl- und Aethylalcohols im Thierkörper," *Archiv für experimentelle Pathologie und Pharmakologie* 31 (1893): 281–302; "Ueber den oxydativen Abbau der Fettsäuren im thierischen Organismus," ibid. 37 (1896): 413–425.

55. F. Hofmeister, "Ueber die Bildung des Harnstoffs durch Oxydation," ibid. 37 (1896): 426–444; "Ueber Methylierung im Thierkörper," ibid. 33 (1894): 198–215.

56. A nearly complete list of the papers published from Hofmeister's successive laboratories in Prague, Strassburg and Würzburg was prepared by Pohl and Spiro (note 47).

57. For appreciations of the important role of Felix Hoppe-Seyler (1825–1895) in the emergence of physiological chemistry during the nineteenth century, see E. Baumann and H. Kossel, "Zur Erinnerung an Felix Hoppe-Seyler," *Zeitschrift für physiologische Chemie* 21 (1895): i–lxi and H. Thierfelder, *Felix Hoppe-Seyler* (Stuttgart 1926).

58. Archives du Bas-Rhin, Strasbourg, AL103, Paquet 194 no. 1028; Paquet 258 no. 1208.

59. See R. von Zeynek, "Gustav Hüfner 1840–1908," *Zeitschrift für physiologische Chemie* 58 (1908): 1–38; A. Wankmüller, "Die Professoren und Dozenten der Physiologischen Chemie in Tübingen," in A. Hermann and A. Wankmüller (Eds.), *Physik, Physiologische Chemie und Pharmazie in Tübingen* (Tübingen 1980), 41–77.

60. Eugen Baumann (1846–1896) was Professor of Chemistry at Freiburg in Breisgau. See A. Kossel, "Eugen Baumann," *Zeitschrift für physiologische Chemie* 23 (1897): 1–22 and M. Spaude, *Eugen Albert Baumann* (Zurich 1973).

61. Pohl and Spiro (note 47), 14.

62. Archives du Bas-Rhin, Strasbourg, AL103, Paquet 259 no. 1211.

63. F. Hofmeister, "Einiges über die Bedeutung und den Abbau der Eiweisskörper," *Archiv für experimentelle Pathologie und Pharmakologie* (1908) Suppl., 273–281.

64. F. Hofmeister, *Die chemische Organisation der Zelle* (Braunschweig 1901); see R. E. Kohler, "The Enzyme Theory and the Origins of Biochemistry," *Isis* 64 (1973): 181–196 and M. Florkin, *A History of Biochemistry* (Amsterdam 1975) Part III, p. 26.

65. F. Hofmeister, "Vom chemisch-morphologischen Grenzgebiet," *Zeitschrift für Morphologie und Anthropologie* 18 (1914): 717–724.

66. F. Hofmeister, *Chemische Steuerungsvorgänge im Tierkörper* (Strassburg 1912); "Über qualitativ unzureichende Ernährung," *Ergebnisse der Physiologie* 16 (1918): 1–39, 510–589.

67. F. Hofmeister, "Willy Kühne," *Berichte der deutschen chemischen Gesellschaft* 33 (1900): 3875–3880.

68. Karl Spiro (1867–1932) later became Professor of Physiological Chemistry at Basel; see L. Asher, "Karl Spiro," *Ergebnisse der Physiologie* 34 (1932): 1–17. Max Koppel (1890–1916) was a promising medical student, killed in action during the First World War. Their joint paper, M. Koppel and K.

Spiro, "Über die Wirkung von Moderatoren (Puffern) bei der Verschiebung des Säure-Basengleichgewichts in biologischen Flüssigkeiten," *Biochemische Zeitschrift* 65 (1914): 409–439 has been translated into English by A. Roos and W. F. Boron, "The Buffer Value of Weak Acids and Bases . . . ," *Respiration Physiology* 40 (1980): 1–32.

69. J. Parnas, "Über fermentative Beschleunigung der Cannizzaro'schen Aldehydumlagerung durch Gewebssäfte," *Biochemische Zeitschrift* 28 (1910): 274–294. Parnas came to Hofmeister after receiving his Ph.D. (1908) in organic chemistry with Willstätter. He later became the leader of an important Polish school of biochemistry and made decisive contributions to the study of intermediate carbohydrate metabolism; see C. Lutwak-Mann and T. Mann, "The Parnas School," *Trends in Biochemical Sciences* 6 (1981): 309–310.

70. F. Knoop, *Der Abbau aromatischer Fettsäuren im Tierkörper* (Freiburg 1904). For biographical notices about Franz Knoop (1875–1946) see K. Thomas, "Franz Knoop zum Gedächtnis," *Zeitschrift für physiologische Chemie* 283 (1948): 1–8 and P. Ohlmeyer, "Probleme des Zwischenstoffwechsels: Gedenkblatt für Franz Knoop," *Angewandte Chemie* 60 (1948): 29–33.

71. Between 1901 and 1908 many of these papers appeared in a journal that Hofmeister founded, *Beiträge zur chemischen Physiologie und Pathologie: Zeitschrift für die gesamte Biochemie*. In the absence of adequate documentation, his reasons for establishing this journal are unclear; one possibility is that his associates had encountered difficulties in gaining access to the *Zeitschrift für physiologische Chemie*, although many of the Strassburg papers appeared there between 1897 and 1901. Hofmeister's journal ceased publication because he decided to merge it with the *Biochemische Zeitschrift*, founded in 1906 by Carl Neuberg (1877–1956).

72. The two quotations are from pp. 76–77 and 161–162 of the typescript of Henderson's unpublished *Memories*, written at about 1936–1939, and deposited in the Harvard University Archives (HUG 4450.7.2). I am greatly indebted to Henderson's son, Lawrence J. Henderson, for permission to quote selected passages from this autobiographical memoir, and to Clark A. Elliott, Associate Director of the Archives, for making it available to me for perusal. A description of the Henderson papers has been prepared by J. Parascandola, "Notes on Source Materials: The L. J. Henderson Papers at Harvard," *Journal of the History of Biology* 4 (1971): 115–118. There are many biographical articles about Lawrence J. Henderson (1878–1942); the most extensive one is by W. B. Cannon, *Biographical Memoirs of the National Academy of Sciences USA* 23 (1943): 31–58.

73. See K. Thomas (note 70); K. Boresch, "Friedrich Czapek," *Berichte der deutschen botanischen Gesellschaft* 39 (1921–1922): (97)–(114); P. Ellinger, "Alexander Ellinger 1870–1923," *Ergebnisse der*

Physiologie 23 (1924): 139–179; G. Katsch, "Nachruf für Gustav von Bergmann, *Münchener medizinische Wochenschrift* 97 (1955): 1398–1400; H. J. Deuticke, "Gustav Embden," *Ergebnisse der Physiologie* 35 (1933): 32–48; J. S. Mitchell, "Prof. E. J. Friedmann," *Nature* 178 (1956): 397; P. Hartley, "Henry Stanley Raper 1882–1951," *Obituary Notices of Fellows of the Royal Society* 8 (1952–1953): 567–582.

74. O. Loewi, "An Autobiographical Sketch," *Perspectives in Biology and Medicine* 4 (1960: 1–28. The first of the two major discoveries made by Otto Loewi (1873–1961) was his demonstration in 1902 that an extensively-digested (biuret-free) autolysate of pancreatic protein can replace intact protein in the animal diet. This contribution, clearly related to Hofmeister's earlier work on peptones, together with that of Otto Cohnheim (1873–1953) on the cleavage of peptones by the "erepsin" of intestinal mucosa, provided decisive evidence against the peptone theory of protein synthesis. Loewi's other major achievement, for which he was awarded a Nobel Prize in 1936, was the discovery of the role of the *Vagusstoff* (later identified as acetylcholine) in the chemical mediation of nerve impulses. See F. Lembeck and W. Giere, *Otto Loewi, ein Lebensbild in Dokumenten* (Berlin 1968) and G. L. Geison, *Dictionary of Scientific Biography* (New York 1973) 8: 451–457.

75. K. Spiro, "Franz Hofmeister," *Archiv für experimentelle Pathologie und Pharmakologie* 95 (1922): i–vii.

76. E. Abderhalden, "Franz Hofmeister," *Medizinische Klinik* 18 (1922): 1167–1168.

77. This sketch of the life and personality of Hofmeister is based almost entirely on published material, and may require revision if a major collection of his personal papers is found. Despite an intensive search in Strasbourg, Würzburg and elsewhere, I have located only a dozen of his letters. Perhaps his papers were destroyed during the World War II bombardment of Würzburg, but there appears to be no record of them in the university archives. Of special interest would be Hofmeister's *Tagebuch*, mentioned in Pohl and Spiro (note 47).

78. See G. Embden, "Franz Hofmeister," *Klinische Wochenschrift* 39 (1932): 1974–1975.

79. Letter from Fischer to Baeyer, 5 December 1905, Bancroft Library. For the lecture see E. Fischer, "Untersuchungen über Aminosäuren, Polypeptide und Proteine," *Berichte der deutschen chemischen Gesellschaft* 39 (1906): 530–610. The book was the first in a series of volumes containing Fischer's collected papers and lectures; a collection of his papers in the protein field published after 1906 appeared posthumously (see note 30).

80. In an obituary notice for Albrecht Kossel, A. P. Mathews, *Science* 66 (1927): 293, stated that Fischer's work on the "synthesis of artificial or synthetic proteins" was undertaken "at Professor Kossel's suggestion and request." The validity of

this claim is uncertain, as Fischer had already indicated in 1893 (before Kossel entered the protein field) his interest in "the complete analysis and synthesis of proteins." See E. Fischer, "Antrittsrede . . . ," *Sitzungsberichte der Akademie der Wissenschaften zu Berlin* (1893): 632–636.

81. E. Fischer, "Synthetical Chemistry in its Relation to Biology," *Journal of the Chemical Society* 91 (1907): 1749–1765.

82. M. Bergmann and L. Zervas, "Über eine neue Methode der Peptidsynthese," *Berichte der deutschen chemischen Gesellschaft* 65 (1932): 1192–1201. For an account of the historical background of this method see J. S. Fruton, "The Carbobenzoxy Method of Peptide Synthesis," *Trends in Biochemical Sciences* 7 (1982): 37–39. For Max Bergmann (1886–1944) see C. R. Harington, "Max Bergmann," *Journal of the Chemical Society* (1945): 716–718. The more extensive notice by B. Helferich, "Max Bergmann," *Chemische Berichte* 102 (1969): i–xxvi is inaccurate. For Leonidas Zervas (1902–1980), see P. G. Katsoyannis, *The Chemistry of Polypeptides* (New York 1973), 1–20.

83. It should perhaps be noted that, despite his claims for it, Fischer's ester method did not constitute a quantitative analytical procedure for the determination of the amino acid composition of proteins, since the manipulations made it impossible to recover the individual amino acids in amounts that approximated those in the hydrolysates. No indication was given in Fischer's papers of systematic efforts to estimate the losses that were incurred, for example by adding a known quantity of a given amino acid, and determining whether it could be accounted for in yield of that amino acid at the end of the analytical process. Moreover, most of the proteins employed in Abderhalden's analyses were inhomogeneous materials. Finally, the isolation of the diaminotrioxydodecanic acid by Abderhalden proved to be irreproducible, and in 1913 Fischer withdrew his claim for it as a protein amino acid. For a critical appraisal of the results obtained by Abderhalden in Fischer's laboratory see T. B. Osborne and H. H. Guest, "Hydrolysis of Casein," *Journal of Biological Chemistry* 9 (1911): 333–353.

84. See E. Fischer (note 79), 607–608. The influence of Fischer's suggestion regarding piperazine rings on protein research during the 1920's has been discussed by J. S. Fruton, "Early Theories of Protein Structure," *Annals of the New York Academy of Sciences* 325 (1979): 1–18.

85. Letter, Fischer to Barker, 18 April 1906, Bancroft Library.

86. E. Fischer, "Synthese von Depside, Flechtenstoffe und Gerbstoffe," *Berichte der deutschen chemischen Gesellschaft* 46 (1913): 3253–3288.

87. E. Fischer, *Untersuchungen über Aminosäuren, Polypeptide und Proteine II* (Berlin 1923), 40.

88. F. Hofmeister (note 63). A summary of early efforts to isolate pure peptones may be found in M. Siegfried, *Über partielle Eiweisshydrolyse* (Berlin 1916).

89. W. Ostwald, *Lebenslinien* (Berlin 1927) 2: 111–112.

90. For an example of the popular accounts that appeared after Fischer's 1906 lecture see K. Kautzsch, "Emil Fischers Forschungen auf dem Gebiete der Eiweisschemie," *Umschau* 10 (1906): 129–131.

91. L. J. Henderson (note 72), 75, 85–86.

92. Letter from Fischer to Engelmann, 24 February 1904. Archiv der Humboldt-Universität, Akte 1450, Bl.172–173. This letter is cited by L. Läsker (note 31), 111.

93. H. Schröer, *Carl Ludwig* (Stuttgart 1967); M. Lindemann and S. A. Česnokova, "Der Einfluss der Schule Carl Ludwigs auf die Entwicklung der Physiologie in der zweiten Hälfte des vorigen Jahrhunderts," in Mikulinsky et al. (note 4), 2: 147–154.

94. E. Kennaway, "Some Recollections of Albrecht Kossel," *Annals of Science* 8 (1952): 393–397.

95. The description of the synthesis and properties of the octadecapeptide is written out in one of Axhausen's research notebooks (No. 2, pp. 83–86), included in the Emil Fischer Collection at the Bancroft Library.

96. Nor did I include members of the research groups associated with the *ausserordentlicher Professor* in charge of instruction in inorganic and analytical chemistry, administratively within Fischer's institutes in Würzburg and Berlin. Several of these senior colleagues were organic chemists who had been Fischer students and assistants, for example Ludwig Knorr and Wilhelm Wislicenus.

97. See J. S. Fruton, *A Bio-Bibliography for the History of the Biochemical Sciences* (Philadelphia 1982) and the Supplement to this volume (1985). In the search for biographical data I have been greatly aided by many archivists in German universities, chemical firms, and state and city archives, to all of whom I am deeply grateful for their generous help.

98. At least 15 of Fischer's German students died while in military service during the First World War. One of them was Richard von Grävenitz, who presented his Ph.D. dissertation on 5 August 1914, at once entered the army as befitted the scion of a noble family with many generals, and was killed in action a month before the Armistice. Among the Hofmeister people at least one (Koppel) died while on service in the German army.

99. It is noteworthy that all these men later worked at one of the Kaiser-Wilhelm institutes (Warburg, Franz Fischer, Bergmann), at the Rockefeller Institute for Medical Research (Landsteiner, Levene, Jacobs, Van Slyke, Bergmann), or the Pasteur Institute (Fourneau).

100. The Berlin hospitals (Charité, Moabit) were especially active centers of biochemical research; see G. Sauer, S. M. Rapaport and G. Rost, "Zur Geschichte der Biochemie in Berlin," *NTM* 1 (1961): 119–147.

101. My claim for the disappearance of these individuals from the scientific, medical or technical literature is based on an examination of the following

sources: *Chemisches Zentralblatt, Chemical Abstracts, Royal Society Catalogue of Scientific Papers, International Catalogue of Scientific Literature, Index Medicus, Quarterly Cumulative Index to Current Medical Literature, Quarterly Cumulative Index Medicus.* The search covered a 30-year period after the individual's association with Fischer or Hofmeister.

102. See H. Caro, "Über die Entwicklung der Theerfarben-Industrie," *Berichte der deutschen chemischen Gesellschaft* 25 (1892): 955–1105; L. F. Haber, *The Chemical Industry during the Nineteenth Century* (Oxford 1958); J. J. Beer, *The Emergence of the German Dye Industry* (Urbana 1959); E. Hickel, "Die industrielle Arzneimittelforschung am Ende des 19. Jahrhunderts und die Durchsetzung einer reduktionistischen Biologie," in *Materialistische Wissenschaftsgeschichte* (Berlin 1981), 132–154. For the views of a contemporary industrial employer see C. Duisberg, "The Education of Chemists," *Journal of the Society of Chemical Industry* 15 (1896): 427–431.

103. H. W. Schütt, "Zum Berufsbild des Chemikers im Wilhelminischen Zeitalter," in E. Schmauderer (Ed.), *Der Chemiker im Wandel der Zeiten* (Weinheim 1973), 285–308.

104. See Pohl and Spiro (Note 47), 15.

105. It is of course possible to collect data on the number of papers each of the productive scientists published as an independent investigator, and on the size of the research group he (or she) led, as was done in this essay for Fischer and Hofmeister, but this again could serve only as background for an assessment of the quality and significance of the scientist's efforts in research and education.

106. P. Duden and H. P. Kaufmann, "Ludwig Knorr zum Gedächtnis," *Berichte der deutschen chemischen Gesellschaft* 60A (1927): 1–34; Anon., "Wie die ersten Heilmittel nach Höchst kamen," *Dokumente aus Höchster Archiven* No. 8 (Frankfurt 1965); H. W. Flemming, "Ludwig Knorr, Begründer Höchster wissenschaftlicher Tradition," ibid. No. 31 (Frankfurt 1968).

107. S. Olsen, "Otto Diels," *Chemische Berichte* 95 (1962): v–xlvi. This obituary notice contains excerpts from Diels's unpublished autobiographical memoir, with comments about Fischer's personality and his attitude toward his junior associates.

108. A. Butenandt, "The Windaus Memorial Lecture," *Proceedings of the Chemical Society* (1961): 131–138; W. Hückel, "Adolf Windaus' Bedeutung für die theoretische organische Chemie," *Angewandte Chemie* 59 (1947): 185–188; L. Josephson, "The Story of the Isolation of Crystalline Vitamin D_1," *Journal of the American Pharmaceutical Association* 22 (1933): 309–312.

109. A. Treibs, *Das Leben und Wirken von Hans Fischer* (Munich 1971); C. J. Watson, "Reminiscences of Hans Fischer and his Laboratory," *Perspectives in Biology and Medicine* 8 (1965): 419–435. For Friedrich von Müller (1858–1941) see G. B. Gruber, "Friedrich von Müller—zum Gedächtnis seines 100. Geburtstages," *Medizinische Klinik* 53 (1958): 1589–1595.

110. E. Philippi, "Fritz Pregl," *Microchemical Journal* 6 (1962): 5–16; F. Szabadvary, *History of Analytical Chemistry* (Oxford 1966), 302–303.

111. H. Pichler, "Franz Fischer," *Chemische Berichte* 100 (1967): cxxvii–clviii; J. C. Sowden, "Herman Otto Laurenz Fischer," *Advances in Carbohydrate Chemistry* 17 (1962): 1–14; R. Willstätter, "Carl Dietrich Harries," *Berichte der deutschen chemischen Gesellschaft* 59A (1926): 123–157; W. Hückel, "Otto Ruff," ibid. 73A (1940): 125–156; F. Kröhnke, "Hermann Leuchs," *Chemische Berichte* 85 (1952): lv–lxxxix; H. W. Wanzlik, "Helmuth Scheibler," ibid. 102 (1969): xxvii–xxxix.

112. M. Heidelberger, "Karl Landsteiner," *Biographical Memoirs of the National Academy of Sciences USA* 40 (1969): 177–210; P. Steiser, *Karl Landsteiner* (Vienna 1961); G. R. Simms, *The Scientific Work of Karl Landsteiner* (Zurich 1963).

113. H. A. Krebs, "Otto Heinrich Warburg," *Biographical Memoirs of Fellows of the Royal Society* 18 (1972): 629–699; *Otto Warburg* (Stuttgart 1979, Oxford 1981). The quotations in this section are from the German version of Krebs's book.

114. K. Heyns, "Emil Abderhalden," *Pflügers Archiv für die gesamte Physiologie des Menschens und der Tiere* 253 (1951): 229–237; H. Hanson, "Emil Abderhalden," *Nova Acta Leopoldina* n.s. 46 (1970): 257–317; C. Picco, *Das Biochemische Institut der Universität Zürich* (Aarau 1981), 24–30. A list of Abderhalden's publications is given in the *Jahrbuch der Akademie der Wissenschaft und der Literatur, Mainz* (1951): 163–204.

115. For biographical articles about Bergmann and Zervas see note 82. Some of my recollections of the work in Bergmann's New York laboratory are recorded in J. S. Fruton, "The Education of a Biochemist," in G. Semenza (Ed.), *Of Oxygen, Fuels and Living Matter* (Chichester 1982), Part 2, pp. 315–360. It may be noted that Bergmann's interest in chemical numerology finds early reflection in an article by Emil Fischer, "Isomerie der Polypeptide," *Sitzungsberichte der Kgl. Preussischen Akademie der Wissenschaften* (1916): 990–1008, in which he acknowledges Bergmann's help in the calculations.

116. For Freudenberg see *McGraw-Hill Modern Men of Science* (New York 1968) Vol. 2, pp. 163–165 and K. Freudenberg, "Von Emil Fischer zur molekularen Konstitution der Cellulose und Stärke," *Chemische Berichte* 100 (1967): clxii–clxxviii. For Helferich see H. Bredereck, "Zur Entwicklung der Chemie der Kohlenhydrate und der Glycosidspaltenden Enzyme," *Angewandte Chemie* 69 (1957): 405–412. For Zemplén see O. T. Schmidt, "Géza Zemplén," *Chemische Berichte* 92 (1959): i–xix.

117. M. Delépine, "Notice sur la vie et les travaux de Ernest Fourneau," *Bulletin de la Société Chimique de France* (1950) 5e série 17: 953–982; T. A. Henry, "Ernest Fourneau," *Journal of the Chemical Society*

(1952): 261–266. In a letter to Fischer dated 21 October 1901, Fourneau thanks him for the reprints "du petit travail sur l'anhydride du glycocolle" (Fischer Collection, Bancroft Library).

118. D. D. Van Slyke and W. A. Jacobs, "Phoebus Aaron Theodore Levene," *Biographical Memoirs of the National Academy of Sciences USA* 23 (1944): 75–126; R. C. Elderfield, "Walter Abraham Jacobs," ibid. 51 (1980): 247–278; A. B. Hastings, "Donald Dexter Van Slyke," ibid. 48 (1976): 309–360; E. R. Long, "Harry Gideon Wells," ibid. 26 (1949): 233–261.

119. For accounts of Embden's life and work see H. J. Deuticke (note 73) and C. F. Cori, "Embden and the Glycolytic Pathway," *Trends in Biochemical Sciences* 8 (1983): 257–259.

120. For Friedmann see J. S. Mitchell (note 73). To my knowledge, the only extensive biographical article about Parnas is the one by J. Heller and W. Mozolowski, "Jakub Karol Parnas," *Postepy Biochemii* 4 (1958): 5–65. A list of his publications has been published by I. Mochnacka, *Acta Biochimica Polonica* 3 (1956): 3–39.

121. F. Lieben, "Wolfgang Pauli," *Österreichische Chemische Zeitung* 56 (1955): 336–337; it should be noted that before 1899 Pauli's papers appeared under his former name (Pascheles). For Fürth see F. Lieben, "Otto von Fürth," *Wiener klinische Wochenschrift* 60 (1948): 377–379.

122. H. Molitor, "In Memoriam Ernst Peter Pick," *Archives internationales de pharmacodynamie et de thérapie* 132 (1961): 205–221.

123. J. Kühnau, "Wilhelm Stepp," *Deutsche medizinische Wochenschrift* 89 (1964): 1911–1912. For Raper and Czapek see note 73.

124. O. Riesser, "Julius Pohl zum 70. Geburtstage," *Deutsche medizinische Wochenschrift* 57 (1931): 1869; H. E. Voss, "In Memoriam Prof. Dr. W. S. Loewe," ibid. 89 (1964): 93–94. For Ellinger see note 73.

125. R. Thauer, "Albrecht Bethe," Pflügers *Archiv für die gesamte Physiologie des Menschen und der Tiere* 261 (1955): i–xiv.

126. G. von Bergmann, "Friedrich Kraus," *Deutsche medizinische Wochenschrift* 62 (1936): 482–484; H. Opitz, "In Memoriam Adalbert Czerny," ibid., 88 (1963): 723–725; E. Schiff, "Adalbert Czerny," *Journal of Pediatrics* 48 (1956): 391–399; for Gustav von Bergmann see note 73.

127. I. Zadek, "Magnus-Levy," *Münchener medizinische Wochenschrift* 97 (1955): 834–835; M. G. Goldner, "Adolf Magnus-Levy," *Diabetes* 4 (1955): 422–424; K. Spiro, "Leon Blum," *Schweizerische medizinische Wochenschrift* 60 (1930): 379–380; W. Pilgersdorfer and E. Rissel, "Zum 5. Todestage Professor Hans Eppingers," *Wiener klinische Wochenschrift* 101 (1951): 880–884; A. Hottinger, "Ernst Freudenberg," *Helvetica Paediatrica Acta* 22 (1967): 497–499. In the foregoing biographical sketches I have mentioned the emigration from Germany and Austria of several chemists and medical scientists after Hitler's rise to power. At least 4 chemists (including Fischer's son) and 3 medical scientists from the Fischer group (Appendix 1) and 19 former members of the Hofmeister group (Appendix 2) emigrated, most of them to the United States and England, and a few to Turkey or Israel. See H. Pross, *Die deutsche akademische Emigration nach den Vereinigten Staaten 1933–1941* (Berlin 1955); H. A. Strauss and W. Röder (Eds.), *International Biographical Dictionary of Central European Emigrés 1933–1945* Vol. 2, two parts (Munich 1983).

After this paper had gone to press, I read the recent article by H. A. M. Snelders, "J. J. van't Hoff's Research School in Amsterdam (1877–1895)," *Janus* 71 (1984):1–30. This important study should be added to the contributions of Morrell and Geison, cited in note 6.

APPENDIX 1

The Fischer Research Group

Name, Dates and Nationality*	Association with Fischer	Principal Subsequent Activity
ABDERHALDEN, EMIL (1877–1950)	Post-MD, asst 1902–07 (30)	Prof physiology Halle
Ach, Friedrich (1864–1902)	PhD, asst 1889–98 (7,3a)	Chemical industry (Boehringer)
Ach, Lorenz (1868–1948)	PhD, asst 1892–95 (5,10a)	Chemical industry (Schering)
Alexander, Walter (1871–) *USA*	PhD 1894 (2)	Chemical consultant
Andreae, Edward Philip (1879–1975) *Britain*	PhD 1905 (2)	Chemical consultant
Anger, Gerda	1915–19 (1, 2a)	
Antrick, Otto (1862–1942)	PhD 1884 (3)	Chemical industry (Schering)
Arheidt, Richard (?–1924)	PhD 1887 (2)	Chemical industry (BASF)
Armstrong, Edward Frankland (1878–1945) *Britain*	Post-PhD 1901–02 (6)	Chemical industry (ICI)
Axhausen, Walter (1882–)	PhD, asst 1904–09 (2,10a)	Chemical industry (Freudenberg Co)
Baerwind, Heinrich (1892–1968)	PhD, asst 1915–19 (3)	Chemical industry (Boehringer)
Beensch, Leo (1869–)	PhD, asst 1893–96 (4)	Chemical industry (Wilke-Dörfurt)
Behringer, Carl	PhD 1891 (2)	Private medical practice
Bergell, Peter (1875–)	Post-MD 1902–04 (3)	Res inst K. W. Dresden, Rockefeller‡
BERGMANN, MAX (1886–1944)	Post-PhD, asst 1912–19 (12,9a)	Chemical industry (Höchst)
Besthorn, Emil (1858–1921)	PhD 1882 (2)	Chemistry industry (Höchst)
Bethmann, Fritz (1874–)	PhD 1899 (1, 3a)	
Blank, Paul (1882–)	PhD 1906 (2)	
Blix, Martin (1877–1933) *Sweden*	PhD 1902 (1)	Chemical industry (US Sugar Co)
Blochmann, Richard Hermann (1877–)	1901 (1); PhD Rostock 1902	Chemical consultant (photography)
Blumenthal, Herbert (1885–1952)	PhD 1907 (2)	Govt testing bureau Berlin
Boeckler, August (1871–)	PhD 1892 (1)	Chemical industry (BASF)
Böhner, Reginald (1880–1945) *Canada*	Post-PhD 1910–11 (2)	Prof chemistry Syracuse
Boelsing, Friedrich	PhD 1892 (1)	Chemical industry (Neef & Co)
Bösler, Magnus (1852–1924)	PhD, asst 1880–82 (3,5a)	Chemical consultant
Bosart, Louis William (1874–1947) *USA*	PhD 1898 (1)	Chemical industry (Procter & Gamble)
Brauns, Friedrich Emil (1890–1982)	PhD 1913–15 (4,1a)	Chemical industry (Appleton, Wis)

Name	Degree/dates	Career
Brieger, Walter (1891–)	PhD 1914 (3)	Chemical consultant, history of chem
Bromberg, Otto (1870–)	PhD 1895 (5)	Chemical consultant
Brüning, Gustav von (1864–1913)	PhD 1889 (3)	Chemical industry (Höchst)
Brunck, Rudolph (1867–1942)	PhD 1892 (2)	Chemical industry (IG Farben)
Brunner, Arnold (1880–1940)	PhD 1905 (2)	Chemical industry (Höchst)
Bülow, Karl (1857–1933)	Post-PhD asst 1884–86 (3)	Prof chemistry Tübingen
Bunte, Karl (1878–1944)	PhD 1903 (1)	Prof chem technol Karlsruhe TH
Cahn, Heinz (1892–)	PhD 1913, 19 (1)	Chemical consultant
Carl, Hans (1880–1966)	PhD 1906 (2)	Publisher
Chaplin, Edward Mitchell (1868–1948) *Britain*	PhD 1892 (2)	Govt chemical analyst
Clarke, Hans Thacher (1887–1972) *Britain*	Post-DSc 1912 (0)	Prof biological chem Columbia
Clemm, Hans (1872–1927)	Post-PhD asst 1897–98 (3)	Chemical industry (Zellstoff Fabrik)
Colman, Harold Govett (1866–1954) *Britain*	PhD 1888 (2)	Consultant gas industry
Cone, Lee Holt (1880–1957) *USA*	Post-PhD 1908 (1)	Chemical industry (National Aniline)
Crossley, Arthur William (1869–1927) *Britain*	PhD 1892 (3)	Chemical industry (British Cotton)
Culmann, Julius (?–1930) *USA*	PhD 1889 (3)	Chemical industry (Seigle Corp)
Curme, George Oliver (1888–1976) *USA*	Post-PhD 1914 (1)	Chemical industry (Union Carbide)
Curtiss, Richard Sydney (1863–1944) *USA*	PhD 1892 (2)	Various univ appointments in chem
Dangschat, Paul (1893–)	1919 (1)	Chemical consultant
Degen, Joseph (1861–1942)	PhD 1886 (2)	Chemical industry (Degen & Kuth)
Delbrück, Konrad (1884–1915)	Post-PhD asst 1908–09 (2)	Chemical industry (Bayer)
DIELS, OTTO (1876–1954)	PhD, asst 1899–1904 (12)	Prof chemistry Kiel
Dilthey, Alfred (1877–1915)	Post-PhD asst 1902–03 (2)	Private chemical company
Dörpinghaus, Wilhelm Theodor (1878–)	PhD 1902 (2,1a)	Chemical consultant (mining)
Dyckerhoff, August (1868–1947)	PhD 1894 (1)	Family cement factory
Easterfield, Thomas Hill (1866–1949) *Britain*	PhD 1894 (1)	Dir Cawthron Inst Sci Res New Zealand
Ehrensberger, Emil (1858–1940)	1881 (1a)	Director Krupp works
Ehrhardt, Wilhelm	Post-PhD asst 1878–79 (2)	

APPENDIX 1 (continued)

Name, Dates and Nationality*	Association with Fischer	Principal Subsequent Activity
Einbeck, Hans (1873–)	PhD 1905 (1)	Private chemical laboratory
Elbers, Alfred (1861–1936)	PhD 1884 (3)	Family textile factory
Elsinghorst, Gerhard (1858–1929)	PhD 1884 (2)	Chemical consultant
Evans, Thomas Brown (1863–) *USA*	PhD 1886 (1)	Chemical consultant
Fay, Irving Wetherbee (1861–1936) *USA*	PhD 1896 (2)	Prof chemistry Brooklyn Poly Inst
Felser, Heinrich (1881–)	PhD 1908 (1)	Staff K. W. Inst Textile Res.
Fiedler, Albert (1886–1961) *USA*	PhD 1910 (2)	Chemical consultant
FISCHER, FRANZ (1877–1947)	Post-PhD asst 1909–11 (0)	Dir K. W. Inst Coal Research
FISCHER, HANS (1881–1945)	Post-PhD, MD asst 1909 (1)	Prof chemistry Munich TH
FISCHER, HERMANN OTTO LAURENZ (1888–1960)	Post-PhD asst 1912–14 (4)	Prof biochemistry Toronto, Berkeley‡
Fischer, Wilhelm (1868–)	PhD 1892 (2)	
Flatau, Erich	1909 (2)	
Fodor, Kalman von (1881–1931)	Post-PhD 1914–15 (2,1a)	Govt exp station Budapest
Fogh, Johan Bertil (1865–1925) *Denmark*	Post-PhD asst 1895 (0)	Staff agric college Copenhagen
Forster, Martin Onslow (1872–1945) *Britain*	PhD 1892 (1)	Dir Indian Inst Sci Bangalore
FOURNEAU, ERNEST (1872–1949) *France*	Post-PhD 1901 (2)	Pasteur Institute Paris
Frank, Fritz (1868–1949)	PhD 1896 (2)	Govt testing bureau Berlin
FREUDENBERG, KARL (1886–1983)	PhD, asst 1910–14 (7)	Prof chemistry Heidelberg
Freytag, Paul (1876–)	PhD 1912 (1)	
Fritz, Victor (1872–1926)	PhD 1896 (2)	Chemical industry (Boehringer)
Geiger, Walter (1866–)	PhD 1908 (1)	
Gerlach, Ferdinand (1885–)	Post-PhD asst 1912 (1)	Chemical industry (Schuckerts)
Gerngross, Otto (1882–1966)	Post-PhD asst 1909 (1)	Prof chem technol Ankara‡
Geserick, Arthur (1860–)	PhD 1908 (2)	Private chemical factory
Gevekoht, Heinrich (1858–)	PhD 1833 (3)	
Giebe, Georg (1874–1899)	PhD, asst 1896–98 (4,1a)	
Gluud, Wilhelm (1887–1936)	Post-PhD asst 1909–12 (1,4a)	Dir Inst Coal Technol Dortmund
Göddertz, Bernhard Albert (1888–1916)	PhD 1911 (1,3a)	Chemical industry (Bayer)
Grävenitz, Richard von (1890–1918)	PhD 1914 (2)	

APPENDIX 1 (continued)

Name, Dates and Nationality*	Association with Fischer	Principal Subsequent Activity
Jacobi, Friedrich Wilhelm (1863–)	Post-PhD 1895 (0)	
Jacobi, Hermann	PhD 1891 (3,1a)	
JACOBS, WALTER ABRAHAM (1883–1967) USA	PhD 1907 (3)	Rockefeller Inst Med Res
Jänecke, Ernst (1875–1957)	PhD 1898 (1)	Chemical industry (BASF)
Jennings, Walter Louis (1866–1944) USA	Post-PhD 1893–94 (2)	Prof chemistry Worcester Poly
Jessel, Henry Rose (1867–1933) USA	PhD 1900 (1)	Chemical industry (Seattle)
Joachimoglu, Georg (1887–1979) Greece	Post-MD 1912 (0)	Prof pharmacology Athens
Joedicke, Friedrich (1864–)	PhD 1887 (1)	Chemist asphalt industry
Johlin, Jacob Martin (1884–1954) USA	PhD 1910 (1)	Assoc prof biochem Vanderbilt
Johnson, Theodore (1884–) USA	PhD 1906 (1)	
Jourdan, Friedrich	Post-PhD 1883 (1)	Chemical industry Rome
Kaas, Carl (?–1915)	1906 (1)	Asst chemistry Graz
Kadisade, A. Refik (1892–) Turkey	PhD 1915, 18 (2)	
Kalantharianz, Anuschawan (1867–) Russia	PhD 1898 (2)	
Kall, Henry von der	PhD 1890 (2)	Prof chemistry Tokyo
Kametaka, Tokuhei (1872–1935) Japan	Post-PhD 1909 (2)	
Kauffmann, Hugo (1890–1916)	PhD 1914 (1)	Chemical industry (Höchst)
Kautzsch, Karl (1879–1920)	Post-PhD 1905 (1)	Senior lecturer chemistry Liverpool
Kay, Francis William (1883–1967) Britain	PhD 1908 (3)	
Kempe, Martin (1884–)	PhD 1907 (2)	Govt chem techn inst Berlin
Kempf, Richard (1879–1935)	Post-PhD 1904 (0)	
Kleberg, Werner	PhD 1891 (3)	Hospital chief Berlin‡
Klemperer, Georg (1865–1946)	PhD 1891 (1)	Chemical industry (Höchst)
Klotz, Carl (1862–1938)	Post-PhD asst 1886 (3a)	Chemical industry (BASF)
Knoevenagel, Oscar (1862–1944)	PhD 1887 (2)	Prof chemistry Jena
KNORR, LUDWIG (1859–1921)	PhD, asst (3,1a)	Chemical industry (Kalk Chemie)
Koch, Hermann (1858–1939)	PhD 1883–85 (5)	Staff Roosevelt Hosp New York
Koelker, Arthur Heinrich (1883–1911) USA	PhD 1908 (2)	
Koelker, Wilhelm Friedrich (1880–1911) USA	PhD 1905 (2)	Asst prof chemistry Wisconsin

Köllisch, Anton (1888–1916)	PhD 1911 (1)	Chemical industry (Merck)
Königs, Ernst (1878–1945)	PhD 1903 (3)	Prof chemistry Breslau
Kötzle, Arthur (1865–1930)	PhD 1889 (1)	Chemist leather industry
Kohlrausch, Karl (1862–)	PhD 1889 (2)	
Kopisch, Friedrich (1867–)	PhD 1894 (2)	Landowner
Krämer, Adolf (1883–1914)	PhD, asst 1906–09 (3,1a)	Chemical industry (Bayer)
Kraus, Johann (1869–)	PhD 1895 (2)	
Kropp, Walther (1885–1939)	PhD 1908 (2)	Chemical industry (IG Farben)
Kühlewein, Malte von (1887–)	Post-MD, PhD 1915 (1)	Pharmacologist Utrecht
Kuzel, Hans (1859–1921)	PhD 1883 (6)	Chemical industry (Höchst)
LANDSTEINER, KARL (1868–1943)	Post-MD 1892 (1)	Rockefeller Inst Med Res
Langenwalter, Jacob (1868–1943)	PhD 1892 (2)	Chemical industry (BASF)
Laubmann, Heinrich (1865–1951)	PhD 1888 (2)	Chemical industry (Höchst)
Lawrence, William Trevor (1870–1934)	PhD 1896 (2)	Lecturer chemistry Manchester
Lawson, Thomas Atkinson (1862–1903) *Britain*	Post-PhD 1890 (0)	Various chemical companies
Laycock, William Frederick (1866–1912) *Britain*	PhD 1889 (2)	Chemical consultant (dyes)
LeCount, Edwin Raymond (1868–1935) *USA*	Post-MD 1905 (1)	Prof pathology Rush Med Coll
Lehmann, Fritz Julius (1874–)	PhD, asst 1897–99 (1,5a)	Chemical industry (Bayer)
Lehnert, Hermann	PhD 1880 (1)	Govt patent office Berlin
Lemme, Georg (1865–1925)	Post-PhD 1894 (1)	Chemical industry (Haarmann & Reimer)
Lepsius, Richard (1885–1969)	PhD 1911 (2,1a)	Various govt agencies
LEUCHS, HERMANN (1879–1945)	PhD, asst 1901–04 (3,4a)	Prof chemistry Berlin
LEVENE, PHOEBUS AARON (1869–1940) *USA*	Post-MD 1902 (1)	Rockefeller Inst Med Res
Lipschitz, Werner (1892–1948)	PhD 1915 (2)	Prof pharmacology Frankfurt
Loeb, Walther (1872–1916)	PhD 1894 (2)	PvDz chemistry Berlin
Loeben, Wolf von (1869–1913)	Post-PhD asst 1900–01 (2)	Govt testing bureau Berlin
London, Efim Semenovich (1868–1939) *Russia*	Post-MD 1911 (1)	Prof pathol anatomy Leningrad

APPENDIX 1 (continued)

Name, Dates and Nationality*	Association with Fischer	Principal Subsequent Activity
Lorenz, Henry William Frederick (1871–) USA	PhD 1897 (1)	Chemical consultant (photography)
Lüppo-Cramer, Hinricus (1871–1943)	PhD 1894 (2)	Chemical industry (Gelatin Fabrik)
Luniak, Andrei Ivanovich (1881–1957) Russia	Post-PhD 1909 (1)	Prof chemistry Kazan
Macnair, Duncan Scott (1861–1937) Britain	PhD 1889 (2)	Govt educational inspector
Marko, Dmitri Militiadov (1878–) Russia	Post-PhD 1908 (1)	Chem-Techn Institute Perm
Marx, Max (1868–)	PhD 1891 (2)	Chemical consultant
Matsubara, Koichi (1872–1955) Japan	Post-PhD 1906 (1)	Prof chemistry Tokyo
Mauritz, Alfred (1867–1938)	PhD 1891 (1)	Brewing industry Dortmund
Max, Jules (1882–) France	PhD 1906 (2)	Private chemical company
Mechel, Lucas von (1893–1956)	PhD 1916 (2)	Chemical industry (CIBA)
Meyer, Jacob (1863–)	PhD 1889 (3)	Business manager Fischer institute
Meyer, Paul (?–1914)	PhD 1892 (2)	Chemical industry (Kalle)
Michaelis, Ludwig (1869–)	PhD 1893 (2)	Various chemical companies
Minovici, Stefan (1867–1935) Rumania	PhD 1897 (2)	Prof chemistry Bucharest
Moreschi, Annibale (1886–1931) Italy	Post-PhD 1912 (1)	Chemical industry (Stacchini)
Morrell, Robert Selby (1867–1946) Britain	PhD 1893 (2)	Chemical industry (Manders)
Mouneyrat, Antoine (1870–1952) France	Post-PhD 1900 (2); MD Paris 1902	Assoc prof medicine Paris
	1894 (1); PhD Erlangen 1898	Chemical industry (Geigy)
Müller, Franz (1874–)	PhD 1894 (2)	Chemical consultant
Müller, Hermann (1867–)	PhD 1906 (1)	Asst chemistry Danzig
Mylo, Bruno (1884–1915)	PhD 1887 (2)	Chemical industry (Bayer)
Nastvogel, Oscar (1863–1910)	PhD 1887 (2)	Govt nutrition institute
Neufeld, Karl Albert (1866–1914)	Post-PhD asst 1913–14 (2.1a)	Chemical industry (Wolfener Farbenfabr)
Neymann, Hans von Splawa (1885–1916)		
Niebel, Wilhelm (?–1901)	1896 (1)	
Noth, Hartmut (1892–)	PhD 1917 (2,2a)	
Nouri, Osman (1885–) Turkey	PhD 1917 (2)	
Oerker, Rudolf (1889–1916)	PhD 1914 (2)	
Osa, Adolphe de (1872–) France	PhD 1894 (?)	

Ostmann, Paul (1893–)	PhD 1919 (2)	
Otto, Erich (?–1902)	1902 (1)	
Ou, Ching Ko (1885–) *China*	PhD 1911 (2)	
Passmore, Francis William (1867–1921) *Britain*	PhD 1889–90 (3)	Chemical consultant
Pfähler, Ernst (1890–1981)	PhD, asst 1912–14, 19 (2,5a)	Chemical consultant Argentina
Pfeffer, Otto (1885–1918)	Post-PhD asst 1912–1913 (4)	Govt testing bureau Berlin
Pfülf, August (1862–1921)	PhD 1887 (2)	Chemical industry (Buckau)
Pickel, Max (1861–1933)	PhD 1886 (2)	Chemical industry (Nürnberg)
Piloty, Oskar (1866–1915)	PhD, asst 1889–96 (4,3a)	aoProf chemistry Munich
Pinkus, Georg (1870–1943)	PhD, asst 1893–98 (1,13a)	Chemical consultant‡
Plimmer, Robert Henry Aders (1877–1955) *Britain*	Post-PhD 1902 (1)	Prof biochem St Thomas Hosp Med Sch
Poppenberg, Otto (1876–1956)	PhD, asst 1900–02 (1)	Prof chemistry Charlottenburg TH
PREGL, FRITZ (1869–1930)	Post-MD 1905 (1)	Prof medical chemistry Graz
Rabe, Artur (1889–)	PhD 1919 (1)	Chemical industry (Bayer)
Rahnenführer, Carl (1859–1921)	Post-PhD asst 1885–88 (1,7a)	Chemical industry (Weiler-terMeer)
Ramsay, Henrik (1886–1951) *Finland*	Post-PhD 1908 (1)	Various govt commissions
Rapaport, Max (1889–1915)	PhD, asst 1912–14 (2,2a)	
Raschen, Julius (1863–) *Britain*	PhD 1887 (2)	Chemical industry (United Alkali)
Raske, Karl August Heinrich (1863–)	Post-MD, PhD, asst 1903–09 (8)	
Reese, Ludwig	1883 (1)	
Rehländer, Paul (1869–)	PhD, asst 1892–95 (1,10a)	Various chemical companies
Reif, Johann Georg (1880–1964)	Post-PhD asst 1907–1908 (1)	Govt health institute
Reinbold, Bela (1875–1927)	Post-MD 1905 (1)	aoProf physiol chem Szeged
Reinbrecht, Otto	PhD 1891 (2)	
Reisenegger, Hermann (1861–1930)	PhD, asst 1882–84 (4,3a)	Chemical industry (Höchst)
Reitzenstein, Friedrich (1868–1940)	PhD 1892 (1)	aoProf chemistry Würzburg
Renouf, Edward (1848–1934) *USA*	PhD 1881 (2,1a)	Prof chemistry Johns Hopkins
Reuter, Ferdinand (1879–1942)	Post-PhD asst 1904–06 (1,4a)	Chemical industry (Didier Werke)
Richter, Ernst (1861–1917)	Post-PhD 1893 (0)	Chemical consultant
Ristenpart, Eugen (1873–1953)	PhD 1896 (1)	Govt textile institute
Roder, Anton (1864–1931)	PhD 1887 (2)	Private chemical company
Roeder, Georg (1874–)	Post-PhD 1900–01 (2)	Chemical industry (Gerber Milk Co)

APPENDIX 1 (*continued*)

Name, Dates and Nationality*	Association with Fischer	Principal Subsequent Activity
Roesner, Hans (1886–)	PhD 1911 (2)	Chemical industry (Merck)
Rohde (Davis), Alice (1882–1933) *USA*	Post-MD 1914 (1)	Asst prof several medical schools
Rohmer, Martin (1878–1941)	Post-PhD asst 1900–04 (0)	Chemical industry (Höchst)
Rona, Peter (1871–1945)	Post-MD 1904 (1)	Hospital chief Berlin‡
Rose, Frederick (1867–1932) *Britain*	PhD 1894 (1)	Govt education commission
Rostoski, Otto (1872–1962)	Post-MD 1905 (2)	Hospital chief Dresden
Rudolph, Otto (1864–)	PhD 1888 (1)	Chemical consultant
RUFF, OTTO (1871–1939)	Post-PhD asst 1900 (1)	Prof chemistry Danzig, Breslau
Rund (Schmidt-Rund), Charlotte (1890–1970)	PhD 1916 (1); MD Berlin 1918	Private medical practice
Samuely, Franz (1879–1913)	Post-MD 1905 (1)	aoProf medicine Freiburg
Sasaki, Takaoki (1878–1966) *Japan*	Post-MD 1910 (0)	Hospital chief Tokyo
Sattler, Wilhelm (1859–)	PhD 1890 (1)	Owner dye factory
SCHEIBLER, HELMUTH (1882–1966)	PhD, asst 1908–11 (7)	Prof chemistry Charlottenburg TH
Schenkel, Julius Wilhelm (1878–1967)	PhD 1906 (2)	PvDz Munich TH
Schittenhelm, Alfred (1874–1954)	Post-MD 1904 (1)	Prof medicine Kiel
Schlieper, Adolf (1865–1945)	PhD 1887 (3)	Chemical industry (Baum & Co)
Schlotterbeck, Fritz (1876–1940)	Post-PhD 1903–04 (1)	Chemical industry (Stockhausen)
Schmidlin, Julius (1880–1962)	Post-PhD 1905 (1)	Prof chemistry ETH Zurich
Schmidmer, Eduard (1861–1933)	PhD 1892 (2)	Owner factory Nürnberg
Schmidtmann, Hermann (1868–1919)	PhD 1896 (1)	Owner Kaliwerke Aschersleben
Schmitt, Theodor Friedrich (1859–)	PhD 1889 (2)	Govt agricult exp station Vienna
Schmitz, Wilhelm (1882–1939)	Post-PhD asst 1905–06 (2)	Chemical industry (BASF)
Schneider, Wilhelm (1879–1939)	PhD 1909 (2)	Prof chemistry Jena
Schoeller, Walter (1880–1965)	PhD 1906 (2)	Chemical industry (Schering)
Schotte, Herbert (1897–1950)	PhD 1919 (1)	Chemical industry (Schering)
Schrader, Hans (1887–1982)	PhD 1910 (2)	Chemical industry (Goldschmidt Co)
Schrauth, Walther (1881–1939)	PhD 1906 (2)	Chemical industry (Deutsche Hydrierwerke
Schuler, Josef (1883–1963)	PhD 1910 (1)	Chemical industry (CIBA)
Schulze (Schulze-Forster), Arnold (1882–1946)	PhD 1907 (1)	Govt institute of hygiene
Sembritzki, Kurt (1878–1943)	PhD 1897 (2)	Chemical consultant

Name		
Seuffert, Otto (1875–1952)	Post-PhD 1901 (1)	Chemical industry (Merck)
Severin, Josef (1866–)	Post-MD 1912 (1)	Hospital chief Breslau
Skita, Aladar (1876–1953)	Post-PhD asst 1901–02 (2)	Prof chemistry Hannover TH
Slimmer, Max Darwin (1877–) *USA*	PhD 1902 (2)	Chemical consultant
Smith, William Stanley (1863–) *Britain*	PhD 1891 (2)	Chemical consultant (rubber)
Sonn, Adolf (1882–1957)	PhD, asst 1907–10 (1.7a)	Prof chemistry Königsberg
Speier, Arthur	1895 (2); PhD Rostock 1896	Chemical industry (BASF)
Sperling, Rudolf (1888–1914)	PhD 1913 (1)	
SPIRO, KARL (1867–1932)	PhD 1889 (1)	Prof physiological chem Basel
Stahel, Rudolf (1866–)	PhD 1891 (5)	Chemical industry (Sydowsawe)
Stahlschmidt, Alex (1882–1966)	PhD 1910 (2)	Chemical industry (Bayer)
Steche, Albert (1862–)	PhD 1887 (3)	Chemical industry (Heine & Co)
Steingroever, Joseph (1884–)	PhD 1907 (2)	Chemical industry (Deutsche Oxyhydrierges)
		Landowner
Stewart, Anthony *USA*	PhD 1892 (1)	Hospital chief Berlin
Strauss, Hermann (1884–)	Post-MD 1912 (3)	Prof chemistry Tokyo
Suzuki, Umetaro (1874–1943) *Japan*	Post-PhD 1904–05 (5)	Govt patent office Berlin
Täuber, Ernst (1861–1944)	Post-PhD asst 1884 (2a)	Prof chemistry Würzburg
Tafel, Julius (1862–1918)	PhD, asst 1884–89 (9)	Zeiss-Ikon AG
Tappen, Hans (1879–1969)	Post-PhD asst 1906–07 (4a)	
Techow, Walter (1870–)	PhD 1894 (1)	Kitasato Inst Tokyo
Teru-uchi, Yukata (1873–1936) *Japan*	Post-MD 1905 (1)	Pulverfabrik Troisdorf
Thieme, Bruno	PhD 1891 (2)	Asst prof chem Harvard
Torrey, Henry Augustus (1871–1910) *USA*	Post-PhD 1898 (1)	
Trenkler, Bruno	PhD 1887 (2)	Gen Sec German Pharmaceutical Soc
Troschke, Hermann Oswald (1851–)	Post-PhD asst 1879–80 (2)	Rockefeller Inst Med Res
Tüllner, Hermann (1879–1948)	PhD 1902 (2)	
Unna, Eugen (1885–1958)	PhD 1911 (1)	
VAN SLYKE, DONALD DEXTER (1883–1971) *USA*	Post-PhD 1911 (1)	
Voss, Arthur (1882–1940)	PhD 1908 (1.1a)	Chemical industry (Höchst)
Wagner, Philipp (1863–)	PhD 1887 (2)	Private chemical company

APPENDIX 1 (*continued*)

Name, Dates and Nationality*	Association with Fischer	Principal Subsequent Activity
	1891 (0)	
Wagner, Theodore Brentano (1867–1936) *USA*		Various food companies
WARBURG, OTTO (1883–1970)	PhD 1904–05 (3)	K. W. Inst Cell Physiology
Weichhold, Oskar (1883–1965)	PhD 1909 (1)	
Weigert, Fritz (1876–1947)	Post-PhD asst 1902 (1)	Prof photochemistry Leipzig
Weil, Albert (1867–)	Post-PhD 1892 (0)	Chemical industry Görlitz
Weil, Hugo (1863–)	PhD 1885 (2)	Chemical industry (Höchst)
Weller, Heinrich (1853–1923)	Post-PhD 1883 (0)	Govt food res inst
WELLS, HARRY GIDEON (1875–1943) *USA*	Post-MD 1905 (1)	Prof pathology Chicago
Wenzing, Max	PhD 1887 (1)	PvDz Chemistry Graz
Wheeler, Alvin Sawyer (1866–1940) *USA*	Post-PhD 1910 (1)	Prof chemistry North Carolina
WINDAUS, ADOLF (1876–1959)	Post-PhD 1900 (2)	Prof chemistry Göttingen
Wirthle, Ferdinand (1873–1936)	PhD 1890 (1)	Govt food res inst
Wislicenus, Wilhelm (1861–1922)	PhD, asst 1883–85 (1.2a)	Prof chemistry Tübingen
Wolfes, Otto (1877–1942)	Post-PhD asst 1900–01 (1.6a)	Chemical industry (Merck)
Wrede, Franz (1877–1946)	PhD, asst 1903–07 (3)	Chemical industry (Schering)
Zach, Karl (1888–1968)	PhD, asst 1910–13 (5)	Chemical industry (Schuster & Wilhelmy)
ZEMPLÉN, GÉZA (1883–1956)	Post-PhD 1908–1910 (8)	Prof chemistry Budapest
Zöllner, Clemens (1884–)	PhD 1908 (1)	Chemical industry (Schering)

* The names in capital letters denote those who achieved considerable distinction. The absence of a date of death for persons born prior to 1900 indicates only that I have not been able to ascertain the date, and is not to be construed as an affirmation that the person is still alive, where this is not a reasonable assumption. The nationality is indicated only if other than German, Austrian or Swiss.
† PhD refers to a dissertation based on work in Fischer's Institute, the year(s) to the approximate time of association, and the figures in parentheses to the number of publications (including dissertations) as author or co-author; the papers in which Fischer made acknowledgement are indicated separately, *e.g.* 3a.
‡ Emigrated 1933–1945.

APPENDIX

The Hofmeister Research Group

Names, Dates and Nationality*	Association with Hofmeister†	Principal Subsequent Activity
Alexander, Franz (1872–)	Post-MD 1898 (1); asst otolaryng	Private medical practice
Almagia, Marco (1876–) Italy	Post-MD 1906 (2)	Prof physiology Rome
Alzona, Federico (1888–1958) Italy	Post-MD 1914 (1)	Hospital chief Bologna
Auer, Aloys (1888–1948)	MD 1918 (1)	Hospital chief Frankfurt
Baer, Julius (1876–1961)	MD 1899 (2)	Private medical practice‡
Barrenscheen, Hermann Karl (1887–1958)	Post-PhD 1913 (1)	Hospital chief Salzburg
Bassermann, Heinrich (1886–1965)	PhD 1912 (1)	Owner preserves factory
Bauer, Friedrich Alfred (1883–1957)	MD 1907 (1)	Private medical practice
Baum, Fritz (1872–1939)	Post-PhD 1903 (1)	Director chemical factory Barmen
Baumann, Arno (1877–)	Post-MD 1913 (1)	Private medical practice
Bayer, Kurt (1888–)	MD 1915 (1)	Private medical practice
BERGMANN, GUSTAV von (1878–1955)	MD 1902; asst 1902–03 (1)	Prof medicine Berlin
Bernert, Richard	Post-MD 1898 (1)	Private medical practice
BETHE, ALBRECHT (1872–1954)	Post-PhD, MD 1905 (1); asst physiol	Prof physiology Frankfurt
BLUM, LÉON (1878–1930) France	MD 1901; asst 1901–04 (3)	Prof medicine Strasbourg
Blumenthal, Franz (1878–1971)	MD 1903 (1)	Prof dermatol Berlin, Michigan‡
Bonanni, Attilio (1869–1938) Italy	Post-MD 1902 (1)	Prof pharmacology Rome
Brion, Albert (1874–1936) France	MD 1898 (1)	Hospital chief Strasbourg
Bürger, Max (1885–1966)	Post-MD 1916 (1)	Prof medicine Bonn, Leipzig
Comessatti, Guiseppe (1880–1964) Italy	Post-MD 1907 (1)	Docent pathology Padua
Conradi, Heinrich (1876–)	Post-MD 1902 (2)	Hospital chief Zwickau
CZAPEK, FREIDRICH (1868–1921)	MD 1893 (1)	Prof botany Prague
CZERNY, ADALBERT (1863–1941)	MD 1888 (1)	Prof pediatrics Breslau, Berlin
Dauwe, Ferdinand (1881–1948) Belgium	Post-MD 1905 (1)	Prof medicine Ghent
Dietrich, M. Russia	Post-MD 1909 (1)	
Dittrich, Paul (1859–1936)	Post-MD 1891 (1)	Prof legal medicine Prague
Ducceschi, Virgilio (1871–1952) Italy	Post-MD 1902 (1)	Prof physiology Rome
Ebbecke, Ulrich (1883–1960)	Post-MD 1908 (1)	Prof physiology Bonn

APPENDIX 2 (continued)

Names, Dates and Nationality*	Association with Hofmeister†	Principal Subsequent Activity
Ehrmann, Rudolf (1879–1955)	MD 1903 (1)	Hospital chief Berlin
Elias, Herbert (1885–1975)	Post-MD 1913 (1)	aoProf medicine Vienna‡
ELLINGER, ALEXANDER (1870–1923)	Post-PhD, MD 1897 (1)	Prof pharmacology Frankfurt
EMBDEN, GUSTAV (1874–1933)	Post-MD, asst 1899–1903 (6)	Prof vegetative physiol Frankfurt
Emerson, Robert Leonard (1872–1951) USA	Post-MD 1901–02 (2)	Forensic medicine
EPPINGER, HANS (1879–1946)	Post-MD 1905 (3)	Prof medicine Vienna
Falk, Fritz (1878–1912)	Post-MD 1908 (2)	
Filosofov, Petr Ivanovich (1879–1935) Russia	Post-MD 1910 (1)	Hospital chief Leningrad
Fränkel, Sigmund (1868–1939)	Post-MD 1903 (1)	aoProf medical chemistry Vienna
Frank, Armando (1885–1951)	Post-MD 1913 (1)	Hospital chief Leipzig
Freise, Eduard (1882–1921)	Post-MD, asst 1910–12 (1)	Hospital chief Essen
FREUDENBERG, ERNST (1884–1967)	Post-MD 1912 (1)	Prof pediatrics Marburg, Basel‡
FRIEDMANN, ERNST (1877–1956)	PhD, MD, asst 1902–07 (8)	Hospital chief Berlin‡
FÜRTH, OTTO von (1867–1938)	Post-MD, asst 1894–1905 (21)	Prof physical chemistry Vienna
Fuld, Ernst (1873–1955)	Post-MD 1900–02 (3)	Private medical practice‡
Githens, Thomas Stotesbury (1878–1966) USA	Post-MD 1904 (1)	Pharmaceut industry
Glässner, Karl (Charles) (1876–1944)	Post-MD 1902 (6)	Hospital chief Vienna‡
Goldschmidt, Franz (1869–)	MD 1898 (1)	
Goldschmidt, Max (1884–1972)	MD 1910 (1)	Private medical practice‡
Goodman, Edward Harris (1880–1939) USA	Post-MD 1907 (1)	Private medical practice
Granström, Eduard Andreevich (1879–) Russia	Post-MD 1908 (2)	Tuberculosis research
Gross, Alfred (1876–1904)	MD 1899 (1)	
Gümbel, Theodor (1879–1938)	MD 1903 (1)	Private medical practice
Haake, Bruno (1874–)	1902 (1); MD Leipzig 1905	Private medical practice
Haas, Georg (1886–1971)	Post-MD, asst 1912–1916 (2)	Prof medicine Giessen
Halsey, John Taylor (1870–1951) USA	Post-MD 1898 (1)	Prof pharmacology Tulane
Hanssen, Olav Mikal (1878–1965) Norway	Post-MD 1908–09 (2)	Prof medicine Bergen

Name		
(fragment at page top)	1899 (4); MD Vienna 1901	*(faint/cut) … 1903)*
Hausmann, Walther (1877–1938)	Post-MD 1910–14 (2)	Private medical practice
Hebting, Josef (1876–1932)	Post-MD, asst 1917 (0)	Private medical practice
Heller, Friedrich (1883–1963)	Post-MD 1902–04, 08 (2)	Prof biological chemistry Harvard
HENDERSON, LAWRENCE JOSEPH (1878–1942) USA	Post-MD 1904 (1)	
Hildebrandt, Paul (1877–)	MD 1903 (2)	aoProf medicine Berlin‡
Hirsch, Rahel (1870–1953)	Post-MD 1906 (1)	Hospital chief Berlin
Hoesslin, Heinrich von (1878–1955)	Post-MD 1908 (2)	Private medical practice
Hohlweg, Hermann (1879–1941)	Post-MD 1906 (1)	Prof medicine Tokyo
Inada, Ryokichi (1874–1950) *Japan*	MD 1904 (2)	Hospital chief Frankfurt
Isaac, Simon (1881–1942)	1910–11 (1); MD Tokyo 1916	Prof physiology Aichi
Ishimori, Kuniomi (1874–) *Japan*	Post-MD 1900 (3)	Hospital chief Berlin
Jacoby, Martin (1872–1941)	Post-PhD 1900 (1)	Pharmacist
Jochem, Emil (1873–1943)	MD 1886 (1)	
Kauder, Gustav	Post-PhD 1904 (1)	
Kelly, Agnes (1875–) *Australia*	Post-MD, asst 1901–1904 (2)	Prof physiological chem Tübingen
KNOOP, FRANZ (1875–1946)	Post-MD 1910 (2)	Hospital chief Tokyo
Kondo, Kura (1876–) *Japan*	MD 1914 (1)	
Koppel, Max (1890–1916)	Post-MD 1887–89 (2)	Prof medicine Berlin
KRAUS, FRIEDRICH (1858–1936)	MD 1899 (1)	
Krieger, Hans Theodor (1874–)	Post-MD 1898 (2)	Prof physiological chem Kharkov
Kuraev, Dmitri Ivanovich (1869–1908) *Russia*	Post-MD 1899 (1)	Prof ophthalmology Frankfurt
Landolt, Hans Robert Georg (1865–1932)	Post-MD 1894, 1904 (5)	Institute of physiology Budapest
Lang, Sandor	Post-MD 1896 (1)	Prof pediatrics Prague
Langer, Josef (1866–1937)	Post-MD, PhD, asst 1900–03 (7)	Head govt pediatrics institute
Langstein, Leo (1876–1933)	MD 1887 (1)	
Lewith, Siegmund	Post-MD 1906 (1)	Private medical practice
Leibermeister, Gustav (1879–1943)	Post-MD 1894 (1)	Hospital chief Prague
Lieblein, Victor (1869–1939)	Post-MD 1888–92 (3)	Hospital chief Vienna
Limbeck, Rudolf von (1861–1900)	Post-MD 1912–13 (1)	Hospital chief Basel
Löffler, Karl Wilhelm (1887–1972)	MD, asst 1905–10 (3)	Prof pharmacology Göttingen, Dorpat‡
LOEWE, WALTER SIEGFRIED (1884–1963)		

APPENDIX 2 (continued)

Names, Dates and Nationality*	Association with Hofmeister†	Principal Subsequent Activity
LOEWI, OTTO (1873–1961)	Post-MD 1897 (1)	Prof pharmacology Graz‡
Lopez-Suarez, Juan (1884–) Spain	Post-MD 1912–13 (2)	Prof public health Madrid
Lotmar, Fritz (1878–1964)	MD 1904 (1)	Private medical practice
Luzzatto, Riccardo (1876–1922) Italy	Post-MD 1904–06 (2)	Prof pharmacology Modena
Maas, Otto	Post-MD 1900 (1)	Staff, Moabit Hospital Berlin
Magnus-Alsleben, Ernst (1879–1936)	MD 1903 (1)	Prof medicine Würzburg‡
MAGNUS-LEVY, ADOLF (1865–1955)	Post-MD, PhD 1900 (1)	Hospital chief Berlin‡
Mancini, Stefano Italy	Post-MD 1908–09 (3)	Hospital chief Livorno
Meyer, Hans (1877–1964)	Post-MD 1908 (1)	Hospital chief Bremen
Meyer, Kurt (1882–)	MD 1905 (1)	Hospital chief Berlin
Meyer, Max (1890–1954)	MD 1914 (1)	aoProf otolaryngology Würzburg‡
Mochizuki, Jun-ichi (1859–) Japan	Post-MD 1902 (1)	Private medical practice
Morawitz, Paul (1879–1936)	Post-MD 1904 (1)	Prof medicine Greifswald
Münzer, Egmont (1865–1924)	Post-MD 1896 (1)	aoProf medicine Prague
Oseki, Sakaye (1881–) Japan	Post-MD 1914 (1)	Prof pediatrics Osaka
Oswald, Adolf (1870–1956)	Post-MD 1897–99 (1)	Prof medicine Zürich
PARNAS, JACOB (1884–1949) Poland	Post-PhD, asst 1908–1915 (8)	Prof medical chemistry Lwow
Pascucci, Olinto Italy	Post-MD 1905–06 (3)	
PAULI (PASCHELES), WOLFGANG (1869–1955)	MD 1893 (1)	Prof colloid chemistry Vienna‡
Pemsel, Wilhelm (1873–)	Post-PhD 1898 (1)	Hospital chief Graz
Petry, Eugen (1873–1945)	Post-MD 1900 (1)	Prof pediatrics Graz, Munich
Pfaundler, Meinhard von (1872–1947)	Post-MD 1900 (2)	Private medical practice
Pfeiffer, Wilhelm (1879–1937)	Post-MD 1906–07 (2)	Private medical practice
Philippson, Paula (1874–1949)	1902 (1); MD Breslau 1904	Govt testing office Berlin
Picard, Martin 1879–1945)	PhD 1911 (1)	Prof pharmacology Vienna‡
PICK, ERNST PETER (1872–1960)	MD, Post-MD 1897–1901 (5)	Prof otolaryngology Prague
Pick, Friedrich Gottfried (1867–1926)	Post-MD 1894 (1)	Prof pharmacology Prague, Breslau
POHL, JULIUS (1861–1942)	MD, asst 1884–96 (15)	aoProf medicine Vienna‡
Pollak, Leo (1878–1946)	Post-MD 1905–06 (2)	Tropical medicine
Pons, Charles (1876–1952) Belgium	Post-MD 1907 (1)	aoProf medicine Vienna‡
Porges, Otto (1879–1968)	Post-MD 1903 (1)	
Prábram, Hans Leo (1874–1944)	Post-PhD 1899 (1)	

Name		Position
RAPER, HENRY STANLEY (1882–1951) *Britain*	1905–06 (1); DSc Leeds 1910	Prof physiology Manchester
Raudnitz, Robert Wolf (1856–1921)	Post-MD 1893 (1)	Prof pediatrics Prague
Reach, Felix (1872–)	Post-MD 1904 (1)	aoProf physiology Vienna
Reh, Alfred (1878–) *France*	MD 1904 (2)	Private medical practice
Reichel, Heinrich (1876–1943)	Post-MD 1905–06 (4)	Prof Hygiene Graz
Reiss, Emil (1878–1923)	Post-MD 1904 (1)	Hospital chief Frankfurt
Renall, Montague Henry (1888–) *Britain*	1913 (1)	
Reye, Wilhelm (1871–1916)	MD 1898 (1)	Hospital chief Hamburg
Rogozinski, Felix (1879–1940) *Poland*	Post-MD 1908 (2)	Prof physiology Cracow‡
Rosell, Max (1876–1938)	MD 1901 (1)	Private medical practice
Rothera, Arthur Cecil Hamel (1880–1915) *Britain*	1904 (1)	Lecturer biochemistry Melbourne
Rücker, Hans (1874–)	MD 1901 (1)	Private medical practice
Rupprecht, Paul (1887–1965)	Post-MD, asst 1917 (0)	Private medical practice
Salomonsen, Knud Ejnar (1883–1950) *Sweden*	Post-MD 1903 (1)	Military medicine
Samuely, Franz (1879–1913)	Post-MD 1902 (1)	aoProf medicine Freiburg
Sasaki, Takaoki (1878–1966) *Japan*	Post-MD 1907 (2)	Prof medicine Kyoto, Tokyo
Savaré, Mario *Italy*	Post-PhD 1907–08 (3)	Pharmaceutical chem Milan
Schickelé, Gustave (1875–1927) *France*	Post-MD 1911 (3)	Prof obs-gyn Strasbourg
Schlesinger, Eugen (1869–)	Post-MD 1904 (1); asst pediatrics	Private medical practice
Schloss, Ernst (1882–1918)	MD 1906 (1)	Private medical practice
Schmidt-Nielsen, Sigval (1877–1956) *Norway*	Post-PhD 1902–03 (2)	Prof chemistry Trondheim
Schneider, Hugo	Post-MD 1902 (1); asst pediatrics	Prof botany Hohenheim
Schroeder, Henry (1873–1945)	Post-PhD 1907 (1)	Private medical practice
Schrumpf, Pierre (1882–) *France*	MD 1905 (1)	aoProf medicine Vienna
Schütz, Emil (1853–1941)	Post-MD 1886–90 (3)	Hospital chief Vienna
Schütz, Julius (1876–1923)	Post-MD 1900 (1)	Prof physiological chem Jena
Schulz, Friedrich Nikolaus (1871–1956)	Post-MD 1897 (2)	Prof hygiene Hamburg
Schwarz, Leopold (1877–1962)	Post-MD 1899–1903 (3)	PvDz urology Vienna
Schwarz, Oswald (1883–)	1905 (1); MD Vienna 1906	Private medical practice
Schwarzschild, Moritz (1881–1933)	MD 1904 (1)	

APPENDIX 2 (continued)

Names, Dates and Nationality*	Association with Hofmeister†	Principal Subsequent Activity
Seyderhelm, Richard (1888–1940)	Post-MD 1918 (1)	Hospital chief Frankfurt
Siegert, Ferdinand (1865–1946)	Post-MD 1902 (2)	Prof pediatrics Cologne
SPIRO, KARL (1867–1932)	Post-PhD, MD, asst 1896–1919 (38)	Prof physiological chem Basel
STEPP, WILHELM (1882–1963)	Post-MD 1909 (1)	Prof medicine Breslau, Munich
Stolte, Karl (1881–1951)	Post-MD 1904–08 (3)	Prof pediatrics Breslau
Stookey, Lyman Brumbaugh (1878–1940) USA	Post-PhD 1904–05 (1)	Prof physiol Southern California
Strada, Ferdinando (1872–1969) Argentina	Post-MD 1906 (1)	Prof pathological anatomy Cordoba
Swain, Robert Eckles (1875–1961) USA	1902 (1); PhD Yale 1904	Prof chemistry Stanford
Tachau, Paul (1887–1967)	Post-MD 1904 (2)	Private medical practice‡
Takagi (Takaki), Kenji (1881–1919) Japan	1908 (2); MD Tokyo 1910	Prof medicine Tokyo
Tanaka, Masahiko (1876–) Japan	Post-MD 1910–12 (2)	Hospital chief Nagasaki
Tauber, Siegfried	1895 (2)	
Tikhmenev, N Russia	1914 (1)	
Umber, Friedrich (1871–1946)	Post-MD 1898–99 (2)	Hospital chief Berlin
Urano, Fumihiko (1870–) Japan	Post-MD 1907 (2)	
Vogt, Hans (1874–1963)	Post-MD 1901 (1)	Prof pediatrics Münster
Wagner, Richard (1887–1974)	Post-MD 1912–14 (2)	Prof pediatrics Tufts‡
Wallerstein, Saly (1878–)	MD 1902 (1)	Private medical practice
Weil, Josef	1893 (1)	
Wieland, Hermann (1885–1929)	MD 1909 (1)	Prof pharmacology Königsberg
Winternitz, Rudolf (1859–)	Post-MD 1889–93 (4)	Prof dermatology Prague
Würtz, Adolf (1873–)	Post-MD 1912 (1)	Private medical practice
Yokota, Kotaro Japan	1904 (1)	Chemist Virchow hosp Berlin
Zunz, Edgard (1874–1939) Belgium	Post-MD 1899 (2)	Prof pharmacology Brussels

* The names in capital letters denote those who achieved considerable distinction. The nationality is indicated only if other than German, Austrian or Swiss; those designated as French were from Alsace, then under German rule.
† MD (or PhD) refers to a dissertation based on work in Hofmeister's institute, the year(s) to the approximate time of association, and the figure in parentheses to the number of publications (including joint papers) from the institute.
‡ Emigrated or died in concentration camp 1933–1945.

Isidor Traube: Physical Chemist, Biochemist, Colloid Chemist and Controversialist

JOHN T. EDSALL*

Professor Emeritus of Biochemistry, Harvard University

Isidor Traube (1860–1943) was a significant figure in the rapid development of physical chemistry during the last two decades of the nineteenth century. His later activity extended into many aspects of biochemistry, pharmacology, and colloid chemistry. His contributions did not rank with those of such major figures as van't Hoff and Arrhenius, but some were both original and important, and his independence of spirit led him to challenge various prevailing doctrines. As we shall see he was a persistent and stubborn controversialist.

Over a period of more than fifty years in research, Traube published some 200 papers in many different journals, on topics that ranged from the application to liquids and solids of the van der Waals equation of state to the mechanisms underlying the actions of narcotics and toxins, and the selective permeability of biological cell membranes. He was author of an early textbook on physical chemistry (1904), and founded and edited an international journal of physico-chemical biology, with a distinguished editorial board. Unluckily that journal began publication in the spring of 1914, and was eventually a casualty of the First World War.

Traube's most original work was probably on the surface tensions of aqueous solutions of organic compounds, and his name is perpetuated in what became known as "Traube's rule," describing the relative potency of successive members of a homologous series of compounds in lowering the surface tension of water—a rule which, with further research, proved to apply to a wide variety of phenomena, and had far-reaching implications for various aspects of chemistry and biochemistry. Traube was indeed perhaps the first person to perceive the class of phenomena now denoted as hydrophobic interactions.[1] He also did fundamental work on the volumes occupied by chemical substances in relation to their structure, in the pure liquid or solid state, and in recognizing and interpreting the volume contraction that occurs when organic liquids dissolve in a large excess of water. As a young man of 23, before Arrhenius had published anything, Traube had composed a paper "Über die Beziehungen einiger für Lösungen und Gase geltender Gesetze zueinander," in which he drew upon the same data used by Arrhenius and van't Hoff to reach conclusions similar to theirs, but evidently by no means identical. However, on the advice of Lothar Meyer, to whom he turned as a mentor, he withheld this paper from publication. Later he engaged in controversy with Arrhenius; Traube was a supporter of the view that electrolytes were ionized, but he disagreed with Arrhenius's interpretation. Traube indeed was al-

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most the only German physical chemist of his time to dissent openly from the concept of electrolytic dissociation, as formulated by Arrhenius and championed by Wilhelm Ostwald and his school. Unlike the situation in England, where the views of Arrhenius were highly controversial,[2] the German school of physical chemistry, from the late 1880s to the first decade of the twentieth century, was dominated by Ostwald and his pupils, and Traube was a lonely dissenter. This, combined (as he believed, probably justly) with the fact that he was Jewish, blocked his appointment to any major professorship at a German university, though it did not prevent him from pursuing his researches actively into his old age, as an "ausserordentlicher Professor" at the Technical Institute in Berlin–Charlottenburg. At the age of 73 he was uprooted by the Nazi revolution, and spent the last ten years of his life in Edinburgh.

EARLY YEARS

He was born on 31 March 1860 in Hildesheim, the oldest son among six children. His father was a prosperous merchant,[3] who would have welcomed his son into the business, but left him free to pursue his scientific interests. Hildesheim was then a largely medieval city of remarkable beauty,[4] which young Traube keenly appreciated. In school he took an intense interest in the natural sciences, especially astronomy, geology, mineralogy, and paleontology, going on expeditions with his teachers to collect minerals and fossils. His school diploma recorded him as outstanding in chemistry and mineralogy, good in physics and mathematics, but not very satisfactory in Latin.

In 1879 he entered the University of Berlin, welcoming the freedom to study as he liked, with no examinations until the doctoral examination at the end. He attended lectures by philosophers, historians, and professors of literature, and continued his scientific

studies in chemistry, physics, geology, mineralogy, and paleontology. Looking back on that time in old age, he lamented that he had rather neglected the opportunity to study mathematics further. The subject was not then considered of any particular importance for a chemist. As he wrote "In view of the later development of chemistry, I have suffered much from this deficiency and have recognized that great freedom in choice of academic studies has its disadvantages as well as its advantages."[5]

His doctoral thesis dealt with the action of cyanogen chloride on amino acids. His thesis director was the distinguished physiological chemist, Eugen Baumann, whom Traube regarded highly as "ein ganz vortrefflicher Mensch."[6] He received the doctorate on 4 August 1882, as he noted in his autobiography, begun exactly 60 years later. His examiners were Hermann von Helmholtz, A. W. von Hoffman, and the historian Theodor Mommsen; certainly an eminent committee. Traube's range of intellectual interests was certainly wide; one wonders what questions Mommsen may have asked him.

A BRIEF SKETCH OF HIS CAREER

After enduring his military service, Traube came to Heidelberg early in 1883, as an assistant to work on acridines with Professor A. Bernthsen, who later became director of an important laboratory at the I. G. Farbenindustrie in Ludwigshafen. Traube had no particular love for organic chemistry, but Heidelberg delighted him. In later years, if his travels took him in that direction, he always arranged at least an overnight stop at "the incomparable city on the Neckar." He attended with enthusiasm the lectures of the philosopher Kuno Fischer and the great chemist Robert Bunsen. According to Traube, Bunsen and Hermann Kopp were at that time almost the only German chemists who worked on problems of physical or theoretical chemistry. Bunsen was then 72 years old;

Traube, writing nearly sixty years later, recalled him vividly as a "robuste Hühne," striding through the streets of Heidelberg with his diminutive friend Kopp. Traube, on his own initiative, was already studying physical chemistry as it was then known, including the recent papers of Raoult and others (he names de Coppet, Rüdorff and Wüllner) which were to have such far-reaching influence on the work of van't Hoff and Arrhenius, and of Traube himself. These interests led him to draft a manuscript, based on the new developments, and to submit it for advice and criticism to Lothar Meyer, whose book "Die Modernen Theorien der Chemie" had greatly influenced him. To the results of that correspondence I return later.

This period in Heidelberg lasted only half a year. Traube was reluctant to take a job in industry, and welcomed the offer of an assistantship at the Agricultural Academy in Bonn-Poppelsdorf with Professor Freitag, who selected him (so Traube says) because he asked for some free time to do his own research. This apparently persuaded the professor that the young man would really work. Indeed it was here that he first embarked on the study of surface tension, which was to develop into what became probably his most notable contribution to science. For measurements he employed not only the rise in capillary tubes of the liquid under study, but also the method of counting and weighing the drops that fell from the orifice of a suitably designed instrument. The latter instrument, the stalagmometer which he did not originate but greatly refined, led him to design a medicinal glass (*Tropfglas*) which allowed a patient to measure out a precisely prescribed dose of a liquid medicine, simply and easily. This became a commercial product, and was sold (according to Traube) on a world-wide basis, except for England, where the conservatives resisted it and stuck to the old dilution procedures. For Traube it provided a valuable source of income for many years. His design of the stal-

agmometer, and of a related apparatus (viskostagonometer) for the measurement of viscosity of liquids, also found use in many chemical, physical, and biological laboratories.

The seven semesters that Traube spent in Bonn, he notes, were among the happiest of his life; and in his autobiography he grew lyrical over the delights of the Rhineland: the river expeditions with friends, the music and gaiety, the charming girls, along with all the excitement of research, and the somewhat boring, but tolerable, routine teaching.

In the summer of 1887, however, he decided that it was time to leave Bonn and seek a position in technology that would relieve his father of the burden of contributing to his support. With a friend from Bonn, Dr. Guido Bodländer, who had been assistant in pharmacology, he set up a technological and nutritional laboratory in Hannover. The most profitable aspect of this enterprise turned out to involve the liquor industry, in particular the manufacture of brandy. Traube found a simple method, based on some of his earlier research, of separating from raw spirits the undesired higher alcohols (fusel oils) from most of the ethanol by "salting out" with potash. This aroused great interest from several manufacturers, in Germany and Sweden, who financed his journeys to Spain to deal with the producers of the spirits. The process proved highly successful, and enabled many small factories for making brandy to operate successfully and profitably for many years. Finally, about 1909, the process was discontinued, apparently due in substantial part to pressure from some of the large-scale distillers, who found other methods more advantageous. Apparently the payments to Traube from the patents involved represented a substantial source of his income for many years, along with what he received for his medicinal *Tropfglas* and the laboratory stalagmometer.

In 1890 Traube and Bodländer dissolved their partnership and closed the laboratory.

Bodländer later held several academic positions, the last as professor in Braunschweig; but he died not long after going there, at the age of 49. Traube was "habilitated" at the Technische Hochschule in Berlin–Charlottenburg, where he remained for over forty years, becoming a Dozent in colloid chemistry and receiving the title of professor in 1900. He remained, however, a professor extraordinarius until he left Germany in 1934. As an "extraordinary" professor he received even as late as 1930, what he bitterly referred to as "the princely salary of 4500 marks, without entitlement to a pension." Presumably he derived income also from his patents and probably from industrial consulting. That such a productive investigator, who had made distinguished contributions, never achieved the status of an *ordentlicher* professor was an anomaly. Traube wrote of the matter with obvious and understandable bitterness, attributing his anomalous status largely to the fact that he was, and remained, a Jew. His controversial views on various subjects—most notably on the interpretation of the Arrhenius ionization theory—also made him an odd character in the eyes of most German physical chemists. Ostwald, as editor of the *Zeitschrift für Physikalische Chemie*, had generally refused Traube's papers, after a single publication in Volume 1 (1887), to which we refer later.[7]

Nevertheless, on Traube's seventieth birthday in 1930, several well-known investigators in the field of colloid and surface chemistry published articles recalling his distinguished achievements in the past and noting his continuing vigorous activity.[8]

In 1933, with the coming of the Nazi revolution, he was barred from entering his laboratory and his situation became intolerable. At the age of 73 he emigrated to Scotland, where British colleagues had come to his aid. They enabled him to continue his work by providing him with a laboratory at Kings Building, Edinburgh University, and also provided funds that enabled him to live

in a comfortable flat near by.[9] He died in Edinburgh on 27 October 1943.

Figure 1 shows a photograph of Traube, about the age of 60.

PIONEER INVESTIGATIONS ON SURFACE TENSION OF SOLUTIONS: FORMULATION OF "TRAUBE'S RULE"

Traube's research on surface tension of aqueous solutions began when he was an assistant in chemistry in Bonn. Already the physicist George Hermann Quincke (1834–1920) in Heidelberg had studied the surface tension of solutions of salts and other electrolytes. Nearly all such substances increased the surface tension of water. Traube turned instead to the study of aqueous solutions of organic compounds, nonelectrolytes, and weak acids or bases. Moreover, in an approach that was apparently unusual in that early era of physical chemistry, he systematically studied aqueous solutions of homologous series of organic compounds, with a hydrocarbon side chain attached to a polar group: alcohols, esters, ketones, fatty acids. In each of these classes he studied a series of compounds, varying the length of the hydrocarbon chain. In addition he examined compounds containing two or more polar groups—ethylene glycol ($HOCH_2CH_2OH$) and some dicarboxylic acids—oxalic, malonic, succinic, maleic, malic and tartaric acids. In his first published studies[10] he found dramatic differences between the behavior of strong electrolytes and that of these compounds containing nonpolar groups. The former, as Quincke had already shown, slightly increased the surface tension when dissolved in water; the latter significantly decreased it, and the magnitude of the decrease, at a given concentration of solute, became progressively greater as the size of the hydrocarbon side chain increased. Traube termed these latter compounds "capillary-active" in contrast to the salts which were "capillary-inactive."

Fig. 1. Isidor Traube, about 1920.

His earlier training in organic chemistry undoubtedly played an important role here, both in leading him to think in terms of structural relations between classes of or-ganic compounds, in relation to their phys-ical properties, and in careful purification of the compounds he studied. In the measure-ment of surface tension, he made use of, and

improved, both the measurement of the rise of the liquid in a capillary tube, and the measurement of the weight of the drops of liquid that fell from the outlet of a suitably designed system of tubing. Neither method was original with Traube, but he applied both with great skill and care. In particular he developed the drop-weight method, by careful design of the apparatus and especially the shape of the outlet where the drops formed, so that he claimed it to be comparable in accuracy to the capillary rise method. It was certainly an easier method to use, and required less scrupulous care on the part of the operator for good results. It led him to his medicine dropper (*Tropfglas*) for measuring out doses of medicine by volume, which has been discussed above.[11]

Traube in fact had a predecessor in the study of surface tension of solutions of organic compounds in water. This was Emile Duclaux (1840–1904), then professor of physics in Lyon, later to be the chief organizer of the Pasteur Institute in Paris and its director after Pasteur's death. Duclaux employed the drop-weight method to study the surface tensions of aqueous solutions of a series of alcohols, from ethanol to amyl and capryl alcohols, and of several fatty acids, and he clearly perceived the striking increase in the capacity of these substances to lower the surface tension of water, the magnitude of the effect increasing markedly with each increase in the length of the hydrocarbon chain.[12]

Duclaux reported relative surface tensions (γ/γ^0), taking the value for water (γ^0) as unity. He made up his solutions by volume, in cm^3 of solute per 100 cm^3 of the resulting solution. This obscured the molar relations that Traube later pointed out. Nevertheless Duclaux noted that the ratio of volume concentrations required for two members of the same homologous series, to produce a given lowering of the surface tension of water, was essentially constant over a wide range of values. Thus, in comparing alcohols, differ-

ing by one CH$_2$ group, he found that the concentration of *n*-butyl alcohol (C$_4$H$_9$OH) required was 2.6–2.8 times as much as the concentration of *n*-amyl alcohol (C$_5$H$_{11}$OH), for all values of relative surface tension from 0.90 to 0.40.

Traube in his most important and comprehensive study of surface tension in relation to structure, (1891), used the capillary rise method. By then he had realized clearly that comparison of solutions of different compounds must be made on a molar basis to give significant relations to structure. He reported on solutions of 38 organic compounds in aqueous solution, in each case for a range of concentrations. For the more soluble compounds he started with a 1 molar solution, and then made dilutions by factors of 2, 4, 8 . . . etc. For compounds with the larger hydrocarbon side chains, the solubility was too low to prepare molar solutions; in these cases the dilutions were extended to molar concentration as low as $^1/_{256}$, or in one case (propylpropionate) to $^1/_{1024}$.

Traube drew no diagrams in this paper to illustrate his data. The immense amount of information in his tables is difficult to assimilate without careful study, and his notation differs somewhat from that of later authors. In Figs. 2 and 3 I have therefore plotted samples of his data, for alcohols and for fatty acids respectively. It is immediately apparent that (in contrast to sodium chloride, at the top of Fig. 3) all the organic compounds studied decrease the surface tension of water. In each curve the surface tension (γ) plotted as a function of the molar concentration (m) approaches a limiting (negative) slope ($d\gamma/dm)_{m\to 0}$. This he termed the molecular cohesion. Traube stated the relation[13]: "In homologous series of capillary-active substances the constant end values of the molecular cohesion of sufficiently dilute solutions stand in the ratio 1:3:3^2:3^3 . . . , the pressure which the dissolved molecules exert on a unit area of surface increases in homologous series of capillary-active sub-
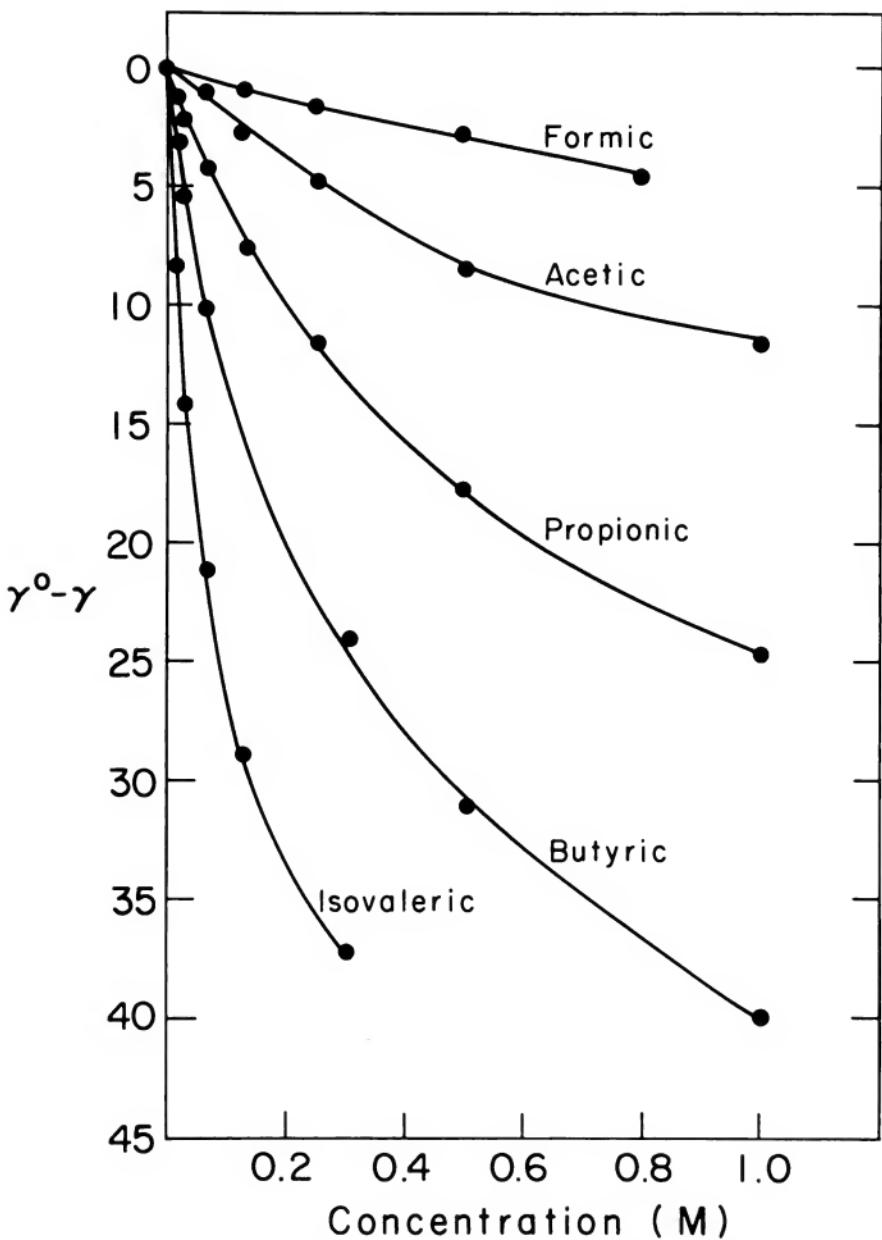
FIG. 2. Surface Tensions of aqueous solutions of some organic acids; data from Traube.[13]
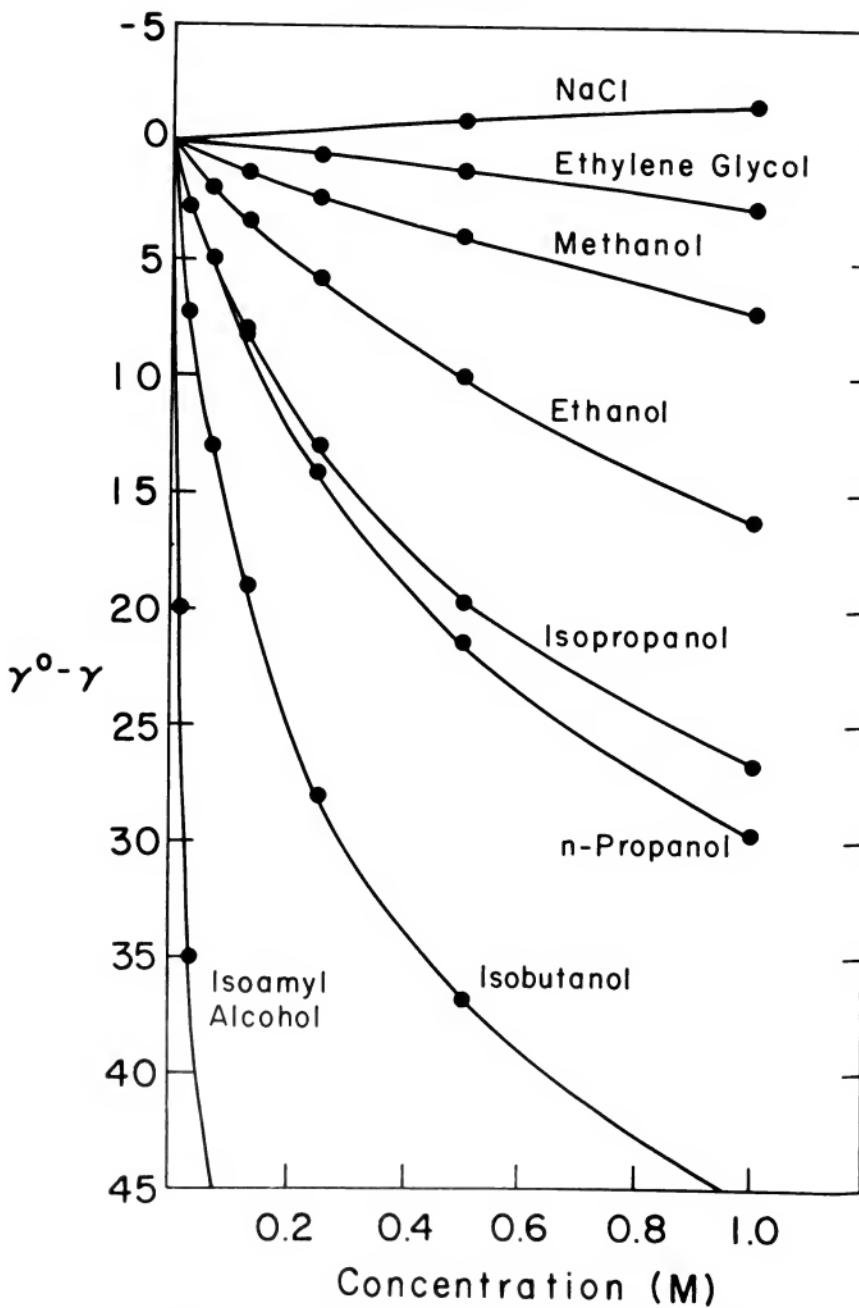
FIG. 3. Surface Tensions of aqueous solutions of some alcohols; data from Traube.[13]

stances, on addition of a CH_2 group, in the ratio $1:3:3^2:3^3...$" (This passage is in italics in the original German.) He did not find such simple relations for compounds containing more than one polar group such as the dicarboxylic acids $HOOC \cdot (CH_2)_n \cdot COOH$, where n is respectively 0, 1, and 2 for oxalic, malonic and succinic acids. These all give small limiting slopes, not far from that for formic acid in Fig. 2.

At higher concentrations the curves in Figs. 2 and 3 (and in Traube's data for esters and other compounds) flatten out and tend to level off. However, as he clearly pointed out, there is a family relation between all the curves; a relation that in fact Duclaux had already clearly pointed out, in terms of volume rather than molar concentrations. If one considers the concentrations of different substances necessary to produce a given lowering in the surface tension of water—this can be done by drawing a horizontal line, at any level, on Fig. 2 or 3, and noting the concentrations at which the line cuts the curves—then it is found that the concentrations decrease, with increasing numbers of CH_2 groups in the molecule, in the ratios 1: $^1/_3:^1/_9:^1/_{27}$ etc. In other words, as Irving Langmuir later pointed out, the curves can all be described by the relation:

$$\gamma - \gamma^0 = f(m/A) \qquad (1)$$

where f is a function that is the same for all molecules in a homologous series, and A is a coefficient that increases by a factor of approximately 3 for each added CH_2 group. Traube illustrates this by a set of tables[14] for 18 of the compounds he studied, over successive intervals of $\gamma^0 - \gamma$. There is no reason, of course, to expect that the factor of 3 should be an integer; some of the numerous ratios listed are as low as 2.7, and a few as high as 3.8, but the approximate constancy is impressive.

Isomeric compounds in water, such as n-butyric and *iso*butyric acids, gave surface tension data that are nearly superimposable;

and the same turned out to be true for isomeric fatty acids and esters containing the same number of carbon atoms; thus propionic acid and methyl acetate, butyric acid and ethyl acetate, etc., gave almost indistinguishable data.[15]

Traube was well aware of the principle, first enunciated by Willard Gibbs, that dissolved substances that lower the surface tension of a solution tend to concentrate at the surface; although, as far as I am aware, he seldom or never applied the Gibbs equation (equation 3 below) for quantitative calculations. He was clearly aware, however, that the relations he discovered required that the substances he studied must increasingly tend to concentrate in the surface layer, as the size of the hydrocarbon chain increased. Traube did not pursue his studies with substances containing much longer hydrocarbon chains; these of course were exceedingly insoluble, and it later became apparent that they would form surface films, which led to a quite different, though closely related, line of research.

For about a quarter of a century Traube's work was apparently largely ignored. In 1908, B. von Szyszkowski, working in Ostwald's laboratory, studied the surface tensions of a series of fatty acids, with results essentially equivalent to Traube's work on the same substances. He developed an empirical equation to fit his data:

$$\gamma^0 - \gamma = B \ln\left(\frac{m}{A} + 1\right) \qquad (2)$$

Here B and A are constants. For a homologous series, B is the same for all members, while A decreases progressively, by a factor close to 3, for each added CH_2 group. This equation has proved useful for describing the data of other workers, including Traube's earlier and far more extensive studies. Szyszkowski, however, gave no reference to Traube, which suggests that Traube's work had largely been forgotten at that time. In-

deed Ostwald, with whom Szyszkowski was working, tended strongly to disparage Traube's work; but a more likely reason is that Szyszkowski was simply unaware of it.[16]

After a quarter century, however, the importance of Traube's work was recognized by Irving Langmuir, who realized its far-reaching implications for the structure of liquids and surface layers.[17] In considering the distribution of a dissolved substance between the interior of a liquid and the surface layer, Langmuir stated the Gibbs equation in the form:

$$q = -\frac{c}{RT}\left(\frac{d\gamma}{dc}\right) = -\frac{1}{RT}\frac{d\gamma}{d\ln c} \quad (3)$$

Here q is the amount of solute adsorbed per cm^2 of surface, and c is the concentration in the interior of the liquid. Taking account of the kinetic equilibrium between the surface layer and the interior, the relation between q and c should be of the form

$$q/c = const. \; e^{\lambda/RT} \quad (4)$$

where λ is the decrease in potential energy that occurs when one mole of solute passes from the interior into the surface layer. Traube's data for a homologous series show that, in dilute solutions, λ increases progressively as a linear function of the number of hydrocarbon groups. In other words the internal potential energy of the solute molecules, when surrounded by water, becomes greater, and their tendency to pass from the interior of the solution into the surface phase increases, the longer the hydrocarbon chain. Thus in the limiting case of very dilute solutions, where Traube's data show that γ is a linear function of the solute concentration, the concentration in the surface layer (c_s) must bear a constant ratio to c_w, the concentration in the interior of the liquid.

Thus, under these conditions, we can write an equilibrium constant K

$$K = c_s/c_w \quad (5)$$

The standard Gibbs free energy of transfer (ΔG^0) per mole of solute, from the interior of the liquid to the surface layer, is then, by a fundamental thermodynamic equation:

$$\Delta G^0 = -RT \ln K = -RT \ln (c_s/c_w) \quad (6)$$

Traube's data show that K increases by a factor of approximately 3 for each added CH_2 group in a homologous series. Thus $RT \ln K$ must increase by the factor RT in 3 when a CH_2 group is added. Taking $R = 1.987$ cal mol^{-1} Kelvin^{-1}, and T as 288 K (15°C) in Traube's experiments, this means that the standard free energy of transfer increases by about 630 calories per mole per CH_2 group added. Table I lists some of Traube's data and Langmuir's recalculations.

In his Nobel Prize lecture in 1932, Langmuir again emphasized the importance of Traube's work, pointing out that the limiting relations for the formation of surface films, at very low and at nearly saturated concentrations of solute "are completely in accord with the general relationships found by I. Traube." Langmuir also noted that the constant increment in Gibbs energy per CH_2 group in a homologous series indicated a similar orientation of the surface molecules in the films at high dilution—presumably with the hydrocarbon side chains oriented horizontally on the water surface.[18]

Langmuir's thermodynamic interpretation of Traube's rule can be applied, not only for transfers of solute molecules from the interior of the solution to a surface phase, but also to their transfer from solution in water to a liquid phase consisting of an organic solvent with considerable hydrocarbon character. This relation is given by solubility measurements for the substance in question, in water and in the organic solvent. The logarithm of the solubility ratio in the two phases is proportional to the standard Gibbs energy of transfer between the phases.

This method is particularly useful when the substances studied are crystalline solids,

TABLE I

Capillary coefficients, F, for depression of surface tension, for various substances, in dilute
aqueous solution at 15°C. The symbol Q denotes the ratio of F values
for the successive substances listed.

Substance	F (Traube)	Q (Traube)	F (Langmuir)	Q (Langmuir)
Formic acid, H COOH	8.2		8.	
Acetic acid, CH₃COOH	24.8	3.0	27.	3.4
Propionic acid, CH₃CH₂COOH	73.2	3.0	77.	2.9
Butyric acid CH₃(CH₂)₂COOH	215.	2.9	230.	3.0
Isobutyric acid C₃H₇COOH	215	1.0	240.	1.0
Isovaleric acid C₄H₉COOH	605	2.8	720.	3.0
Methanol, CH₃OH	10.4		11.	
Ethanol, CH₃CH₂OH	29.9	2.9	33.	3.0
n-Propanol, CH₃(CH₂)₂OH	88.6	3.0	98.	3.0
isoPropanol (CH₃)₂CHOH	88.3	1.0	98.	1.0
isoButanol C₄H₉OH	273.	3.1	310.	3.2
isoAmyl Alcohol, C₅H₁₁OH	738.	2.7	910.	2.9
Methyl acetate, CH₃COOCH₃	79.		85.	
Ethyl acetate, CH₃COOC₂H₅	255.	3.2	270.	3.2
Propyl acetate, CH₃COOC₃H₇	758.	3.0	840.	3.1
Methyl propionate, C₂H₅COOCH₃	232.	3.3	245.	3.4
Ethyl propionate, C₂H₅COOC₂H₅	678.	2.9	745.	3.0
Propyl propionate, C₂H₅COOC₃H₇	1894.	2.8	2050	2.8

F denotes the limiting value of $(\gamma^0 - \gamma)/m$, as m approaches zero.
Data from Traube (note 13). The two columns on the right give Langmuir's recalculations of F and Q from Traube's
data (see Langmuir, note 16, p. 1892). Langmuir tabulated values for all the 38 substances reported by Traube, of
which 18 are listed here. The differences between the Traube and the Langmuir values are relatively small and do
not affect Traube's general conclusions.

which are not too highly soluble in either of the two liquid solvents. Since the two saturated solutions are both in equilibrium with the same crystals, the chemical potential of the solute in both solutions must be the same. Thus McMeekin, Cohn and Weare in 1935 studied the solubility, in water and ethanol at 25°C, of a series of amino acids and related compounds, and observed (among other things) the effect of varying the length of a hydrocarbon side chain. As an example, consider the relation between the two simplest amino acids, glycine (⁺H₃N · CH₂ · COO⁻) and alanine (⁺H₃N · CH(CH₃) · COO⁻) which differ by one CH₂ group. Both, because of the electrically charged groups they carry, are far more soluble in water than in ethanol, but the presence of the added CH₂ group in alanine promotes its solubility in ethanol (S_e) relative to water (S_w). For glycine

$S_e/S_w = 4.07 \times 10^{-4}$; for alanine it is 13.9×10^{-4}. The ratio of the two values is 3.4, the factor by which the added CH₂ group favors solubility in ethanol relative to water. The decrease in the Gibbs free energy of transfer is then RT ln 3.4 = 2.303 RT log 3.4 = 2.3 RT (0.53) = 720 cal/mol, for this particular comparison. The average value, for a series of such comparisons, was a little lower, around 670 cal/mol; for transfers from water to n-butanol, a solvent with a larger hydrocarbon side chain, the average effect of a CH₂ group was larger by about 50 cal/mole. McMeekin, Cohn and Weare recognized clearly that they were studying another aspect of the same phenomenon that Traube had observed. They studied the relative solubilities of alanine and phenylalanine, which differ by a benzene ring in the side chain; the presence of the ring shifted the solubility

ratio, in favor of ethanol relative to water, by a factor of 25, or 1900 cal/mole in the Gibbs energy. thus a phenyl (C_6H_5) group was roughly equivalent to three CH_2 groups in its effect on the solubility ratio and the Gibbs energy of transfer.

One might expect a still larger effect for the transfer of a pure hydrocarbon with no polar groups, between water and a hydrocarbon solvent. Such studies have been made, and Tanford's analysis shows that the average increase in the Gibbs energy of transfer, per CH_2 group added, is 884 cal/mol.[19]

Traube's work on surfaces later greatly influenced his thinking about biochemical problems, especially with regard to the factors that determine the permeability of living cells to chemical reagents. He noted, for instance, that the permeability of red blood cells to reagents such as fatty acids appeared to be affected by the length of the hydrocarbon chain, in essentially the same way that he had found for the lowering of surface tension. We return later to this topic, and to the controversies it aroused between Traube and other workers.

His surface tension studies involved a water-air interface. In biochemical systems the interfaces generally involve a liquid/liquid or a liquid/solid interface. Such systems are technically more difficult to study than those at air interfaces. Apparently the first test of Traube's rule at a liquid/liquid interface was done by his daughter, Sonja Boas-Traube in her doctoral thesis, done in the laboratory of Professor M. Volmer, and published in 1937. She studied the surface tension at the water/benzene interface, in the presence of the series of six fatty acids from formic ($H \cdot COOH$) to caproic ($C_5H_{11} \cdot COOH$); the results could be well described by the Szyszkowski equation (equation 2 above). The factor A in that equation is inversely proportional to the limiting values of the lowering of surface tension at low solute concentrations. For propionic acid and higher members of the

series, the increment in A^{-1} per added CH_2 group lay between 3.3 and 3.9; however formic and acetic acids differed by a factor of only 1.8, and acetic and propionic by 2.3. The difference could be traced to the fact that the higher members of the series exist almost entirely as dimers in the benzene solution; whereas formic acid, with no hydrocarbon side chain, is present in monomeric form, and acetic acid is a mixture of monomers and dimers. This conclusion was verified by a study of the distribution coefficients of the various acids between water and benzene.

Traube's work on surface films of substances containing hydrocarbon groups was probably the first quantitative study of what are now commonly referred to as hydrophobic interactions. He made another important contribution to the study of such interactions as one aspect of his work on molecular volumes, which I discuss in detail below. This was his quantitative study of the volume contraction that occurs when an organic liquid is transferred to solution in a large quantity of water. Other characteristic aspects of such interactions, involving changes of enthalpy, entropy, heat capacity, compressibility, and other properties of such solutions, were discovered later. This field of research is at present extremely active, both theoretically and experimentally, and many points are still controversial and obscure; but they remain outside the scope of the present study.[21]

TRAUBE AND THE LIQUOR INDUSTRY: THE PREPARATION OF PURIFIED BRANDY

As already noted, Traube and his friend Dr. Guido Bodländer in 1887 jointly set up a commercial laboratory in Hannover. Around this time, Bodländer called Traube's attention to the fact that an alcohol-water solution, on addition of certain salts at high concentration, would separate into two liquid phases: an upper phase containing much al-

cohol, with less water and salt, and a lower phase composed chiefly of water and salt, with less alcohol. Traube and O. Neuberg studied the phenomenon quantitatively, using ammonium sulfate as the added salt, determining the composition of both the upper and lower phases, and systematically determining the effects of varying the temperature and the total amount of each component added to the system. This appears to have been one of the earliest quantitative studies of the salting-out effect.[22]

One observation in the course of this work led to important practical results. Traube and Neuberg noted that, whereas ethanol was still present at equilibrium in considerable amounts in the lower, as well as in the upper layer, the higher alcohols (fusel oils) were driven almost completely into the upper layer by the concentrated ammonium sulfate. The longer the hydrocarbon chain of the alcohol, the greater was this separatory effect. The removal of fusel oils, in the preparation of distilled liquors from raw spirits, is an essential step. The salting out procedure proved highly efficacious in industrial operations, especially in the making of brandy, and Traube became deeply involved with the liquor industry after he moved from Bonn to Hannover with Bodländer.

Traube's surface tension measurements (by the drop-weight method) proved an excellent assay procedure for the presence of fusel oils. Potash (KOH) proved the most practically efficient reagent for fractionating the raw spirits and driving the fusel oils almost completely into the upper layer, which was a dark evil-smelling layer of liquid. The process had to be repeated several times, and (for brandy of high quality) supplemented by fractional distillation. Several large distilling companies in Germany and Sweden took up the process, and paid Traube's way to go to Spain to deal with the original producers of the starting material. Clearly, for many years, Traube must have received a substantial income from this industrial con-

nection. The opportunity to visit Spain also delighted him, and he speaks with enthusiasm of that country, of Toledo, Cordoba, Seville, and especially Granada and the Alhambra.[23]

During the 1890s Traube's procedure was widely used in brandy-making, at least in Germany and Sweden. He states that it was particularly well adapted to use by relatively small-scale manufacturers, and was approved by the Ministry of Health. However, after about 25 years of successful operation the process was banned, partly on supposedly medical grounds, but largely (according to Traube) owing to political intrigues by some of the large manufacturers. The net result of this step was apparently to put several thousand small distilleries out of business.

In the laboratory at Hannover, the work on brandy making was evidently Traube's principal concern, while Bodländer was more concerned with nutritional chemistry, including the assay of peptones and related substances.

Traube and Bodländer published two papers together, relating to methods for assay of peptones and related substances by surface tension measurements. As already noted, they dissolved their partnership in 1890, when Traube went to the Technische Hochschule in Berlin. Bodländer was apparently not happy in the years of his partnership with Traube, according to the obituary article on him by Alfred Cohen, and was much happier later when he returned to academic life, in which he achieved distinction before his early death.[24]

MOLAR VOLUMES IN RELATION TO STRUCTURE, APPARENT MOLAR VOLUMES IN WATER SOLUTION; THE COVOLUME CONCEPT AND THE VAN DER WAALS EQUATION

Hermann Kopp (1817–1892), who was a familiar figure to Traube during his months in Heidelberg, had devoted himself over

about half a century to the study of molar volumes, especially of liquids, in relation to their molecular structures. The molar volume is simply the molecular weight divided by the density; the problem of the investigator is not only to obtain pure substances and measure their densities but also to choose the conditions under which to make these measurements, so that the structural relations between different substances will emerge most clearly. Kopp concluded that different substances should be compared at constant pressure. This condition was most readily fulfilled by working at the boiling point of each liquid. Kopp aimed to describe the molar volume (V_m) of a substance by addition of volumes assigned to each constituent atom, but the results he obtained were criticized by various other investigators.[25]

Traube, beginning about 1890, approached the study of molecular volumes differently, working at a fixed temperature, usually 15°C (he later studied the effects of varying temperature). He was interested in salts, acids, and bases, as well as nonelectrolytes, and it was obviously impractical to study salts at their boiling points. Moreover he soon focused particularly on the study of aqueous solutions of these compounds, which gave more regular and consistent relations to structure of the solute than did the volumes of the same compounds in the pure liquid or solid state. He measured what he called the "molecular solution volume", v_m, usually in aqueous solution. Taking (aq) as the quantity of solvent (in grams) that contains one mole of solute (of mass m grams),

v_m is defined by the relation:

$$v_m = \frac{m + aq}{\rho} - \frac{aq}{\rho_0} \qquad (7)$$

Here ρ is the density of the solution and ρ_0 that of the pure solvent. Thus v_m is the volume increment when one mole of solute is added to aq grams of solvent; in more recent work it is usually called the apparent molar (or molal) volume of the solute.[26] The most significant measurements, for structural purposes, are those made in dilute solutions. For nonelectrolytes in such solutions v_m is commonly nearly independent of the concentration. For some salts in dilute aqueous solution—magnesium sulfate or anhydrous zinc sulfate, for instance—v_m is actually negative; the volume of the liquid shrinks when a little salt is added. This fact was already well-known before Traube started his work.

In a large series of studies, comparing groups of closely related compounds, Traube determined the volume increments due to substituting, or adding, various atoms or groups. Thus for instance the increment for an added CH_2 group was on the average 16.1 cm^3/mol at 15°C. This process led him to the set of atomic volumes listed in Table II.

Traube, however, found the observed value of v_m to be always greater than the sum of the atomic volumes, $\sum V_a$, by an amount essentially independent of the size of the molecule, and equal on the average to 12.4 cm^3/mol at 15°C. He spoke of this in 1895 as a dilation factor, but later designated it as the covolume (ϕ) of the molecule. Thus for aqueous solutions he wrote:

$$v_m = \sum V_a + \phi = \sum V_a + 12.4 \qquad (8)$$

In a paper of 1895, he listed, for 66 organic compounds of varied types, observed and calculated v_m values. The latter values fitted the observations within ±1 cm^3/mole for the great majority of these compounds, and only two gave deviations larger than 2.0 cm^3/mole.

For many of the same substances, when they could be studied as pure organic liquids, the molar volumes, V_m, could also be described by summation of the same atomic volumes, and adding to them a larger covolume item, Φ:

$$V_m = \sum V_a + \Phi = \sum V_a + 25.9 \qquad (9)$$

TABLE II

Traube's Atomic Volumes

Atom	Volume (cm³/mol)
Carbon	9.9
Hydrogen	3.1
Oxygen (hydroxyl)	2.3 (or 0.4)*
Oxygen (carbonyl or ether)	5.5
Halogens and CN	13.2
Sulfur (in –SH)	15.5
Sulfur (bound to 0)	10–11.5
Nitrogen (trivalent)	1.5
Nitrogen ("pentavalent")	10.7**
Nitrogen (nitro)	8.5–10.7
Ring decrement	subtract 8.1 for each ring
Naphthalene, etc.	

* If two hydroxyls are on adjacent carbon atoms, as in ethylene glycol, the value for the two oxygens combined is taken as only 2.7 (=2.3 + 0.4). Likewise the two oxygens in a carboxyl group are assigned a volume of 5.9 (5.5 + 0.4), whereas the two in an ester are assigned 11.0 cm³/mole. The low values assigned to oxygen (2.3 or sometimes 0.4) are always for oxygen attached to hydrogen (in OH or –COOH).

** "Pentavalent" nitrogen is, in modern terminology, quadricovalent nitrogen carrying a positive charge. Thus it requires a counter ion (e.g. the chloride ion in an amine hydrochloride) to achieve neutrality, which complicates the estimates for the volume of the nitrogen.

As an example of the use of these equations consider acetamide, CH_3CONH_2; add $2C$ (19.8) + $5H$ (15.5) + one O (5.5) + $1 N$ (1.5) = ΣV_a = 42.3. Adding 12.4 for covolume gives 54.7 cm³/mol. The observed value was 54.8.

The covolume term in this case was larger by some 13.5 cm³/mol than in the aqueous solution. In other words, transfer of a pure organic liquid to dilute solution in water is accompanied by a volume contraction of the same amount.[27] However Traube found the covolume Φ to be much more variable than the ϕ value for v_m. It ranged from about 21 to 29 cm³/mol, even for "unassociated" liquids. "Associated" liquids, such as water and the smaller alcohols and fatty acids, gave substantially smaller Φ values: 9.6 for water, 15.5 for formic acid, 17.2 for ethyl alcohol, for example. The advantage of studying v_m values in aqueous solution was obvious: the covolumes (ϕ) varied little from one compound to another, and were essentially the same for alcohols and fatty acids as for the "unassociated" substances. Presumably the molecules of alcohols or acids, in dilute aqueous solution, no longer associated with one another, but with the water. (In a later era, these associations would be discussed in terms of hydrogen bond formation).[28]

Traube considered that the covolume was not an arbitrary parameter, but rather that it had a fundamental significance in extending the van der Waals equation of state for imperfect gases to liquids and solids. For an external pressure p and volume v, the equation read:

$$\left(p + \frac{a}{v^2}\right)(v - b) = RT \qquad (10)$$

Thus the effective pressure in the interior of the gas is enhanced by the term a/v^2, and the accessible volume for the molecules in the gas is diminished by the term b, which van der Waals set equal to four times the total volume of the molecules themselves. It should be remembered that this equation by no means gives a perfect fit to the behavior of actual gases, though it is a decided improvement on the perfect gas equation, when suitable values of a and b are chosen. The term a/v^2 has the dimensions of pressure—the internal pressure of van der Waals—and Traube took it also for liquids and solids to be the internal pressure, which he called K. For the b term of van der Waals, which in a gas at ordinary pressures is small compared with the total volume v, he made the bold assumption that in a molecular liquid b is given by the sum of the atomic volumes—the term ΣV_a in equations (8) and (9). It immediately follows that the term $(v - b)$ in (10) is equal to the covolume Φ. Moreover the internal pressure K is very large compared to one atmosphere; hence $p + K \cong K$. On these assumptions the van der Waals equation for liquids becomes (using Traube's numerical value)

$K\Phi = RT$

$= 22380 \text{ cm}^3 \text{ atm per mole at } 0°C$

Then $K = 22380/\Phi$. This gives for water (with $\Phi = 9.6$) an internal pressure above 2300 atmospheres; for a typical organic compound (with Φ near 25) a value of the order of 900 atmospheres. Such values were comparable, in order of magnitude, to estimates made by other, quite different methods.

Traube extended the analogy between liquids and gases by determination of covolumes as a function of temperature, by volume studies at 0 and 100°C on a large series of hydrocarbons. For the higher members of the series (C_7H_{16} and above) he found a mean covolume near 24.5 cm^3/mol at 0°, and values ranging from 32 to 35 at 100°, and proposed the equation, for Φ as a function of temperature,

$$\Phi_t = 24.5(1 + 0.00366t)$$

where t is Celsius temperature. Thus he concluded that the temperature coefficient of the covolume of such liquids was, within rather large uncertainties of estimation, equal to the temperature coefficient of expansion of a gas. In other work he extended the van der Waals equation to solids as well as liquids, using somewhat similar arguments.

As far as I am aware, these conceptions of covolumes in liquids and solids found little acceptance among his contemporaries, and in our time they have been practically forgotten. The covolume (v-b), as Traube conceived it for liquids and solids, represented a rather small difference between the two much larger quantities, v and b, and the summation of atomic volumes involved in calculating b was subject to modification according to the exact method used in calculating volumes to be assigned to the various atoms. Traube himself (see below) emphasized the variability of atomic volumes, and their dependence on interactions between adjoining atoms in molecules; so it is scarcely

surprising that his attempt to extend the van der Waals equation to liquids and solids has found few, if any, followers.[29]

THE VARIABILITY OF ATOMIC VOLUMES: THE VIEWS OF TRAUBE AND T. W. RICHARDS

As his work progressed, Traube emphasized increasingly that his postulated atomic volumes were not to be regarded as fixed constants, but rather that the volume of an element when it entered into compound formation depended on its relation to neighboring atoms in that compound. As he stated in his review in 1899:

The vibrational space (Schwingungsraum) occupied by an atom alters, more or less, according to the nature of the atom, from one substance to another, under the mutual influences between the various atoms in the compound. The smaller the attraction between neighboring atoms, the more closely does the vibrational space approach its maximum value. On the contrary, the greater the mutual attraction between the atoms, the more the vibrational space is diminished.

A striking example, which he had already noted elsewhere, was the carbon atom. Its molar atomic volume in diamond is only 3.4 cm^3, yet this value nearly triples, to 9.9 cm^3, when carbon is combined with hydrogen and other atoms in organic compounds. Values for nitrogen were also highly variable; the value of 1.5 cm^3/mol, for trivalent nitrogen, did not hold for nitriles, such as CH_3CN, for which a higher value of 3.3 was apparently required; and ionic nitrogen compounds apparently required a substantially larger value. The small value (2.3) that he had assigned to the oxygen in hydroxyl groups might well be assigned largely to a change in the value for hydrogen; in that case the value for O would be greater than 2.3, and that for H lower than 3.1, in OH.

He repeated this view, more emphatically and compactly, in 1901. "The atomic volume of an element alters from one compound to

another; it is smaller, the greater the attraction of the adjacent atoms."[30]

Unknown to Traube, Theodore W. Richards at Harvard University was thinking along similar lines. In 1902 the first of a series of important papers by Richards appeared on "The possible significance of changing atomic volume." (Significantly, he dropped the word "possible" from the titles of the later papers). The essence of his argument was expressed in one sentence of the summary: "The atomic volume is not constant, but a function of pressure and temperature, and probably of electric stress." From density measurements on a series of metals and their oxides he showed how great was the variation in change of volume when a metal is converted to its oxide. In some cases, notably for sodium and magnesium, the oxide was denser than the metal. Clearly the atomic volume must be a variable quantity to account for such data. In all cases there was a contraction when the volume of the oxide was compared with that of the starting materials, and Richards took the value of this as a relative measure for the attractive interatomic forces in oxide formation.

Richards also proposed to calculate the internal pressure of a substance from the heat capacity (C) at constant pressure and the thermal expansion, under conditions where there was no phase change on heating from temperature t_0 to $t_0 + dt$. As a working hypothesis he used the equation $C \, dt = P \, dv$, where $C \, dt$ was the heat input and $P \, dv$ the work done in thermal expansion, P being the internal pressure. For a series of metals he thus calculated internal pressures ranging from 53,700 atmospheres for sodium to 672,000 for copper (and 4.9×10^6 for diamond).

In his second paper Richards pointed out a close parallelism between the heat developed in compound formation and the volume contraction in the process; on correcting for differences in compressibility, the agreement became still closer. He put forward the hypothesis that atoms themselves should be regarded as compressible—a view that became central to his outlook on these problems.

Richards's third paper dealt primarily with the relation between heats and free energies of reactions, especially those taking place in galvanic cells, as a function of temperature. In its general significance it was probably the most important paper of the series, but the problem of varying atomic volumes was only of secondary importance to the argument, so that I do not discuss it further here.[32]

In his fourth paper, Richards pointed out relations between the volume contraction on compound formation and the compressibility of the elements involved, making use of extensive new data from his own laboratory. For the halides of the alkali metals, the greater the compressibility of the elements, the more negative is ΔV of compound formation. He also pointed out that, in general among related substances, the more volatile substance has the larger molecular volume. Both chemical energy and cohesive attraction exert a compressing effect on solids and liquids; Richards concluded that cohesive attraction was the more important factor. As to compressibility, in the light of the atomic hypothesis, he noted two possible alternatives ". . . either a relatively incompressible atom exists within a compressible space, or else the atom itself is compressible, and in a solid or a liquid comes into contact with its neighbors." He noted that the former hypothesis was the one usually accepted at the time, but he reaffirmed emphatically the alternative view—the atoms themselves should be regarded as compressible.

Richards had by this time become aware of Traube's work, and added a footnote saying: "It is a pleasure to call attention here to the entirely independent work of I. Traube in this direction. By an interesting coincidence he published in Drude's *Annalen*, 5: 550 (20 June 1901), the following statement: 'Das Atomvolumen eines Elementes ändert

sich vielmehr von Stoff zu Stoff; es ist um so kleiner, je grösser die Anziehung zu den benachbarten Atomen ist,' while on 15 June of the same year there appeared in the *Proceedings of the American Academy*, 37: 17, my version of the same relationship: 'The atomic volume is not constant, but a function of pressure and temperature and probably of electric stress.' By *pressure* was meant the internal pressure caused by affinity. In his pamphlet, 'Über den Raum der Atome' [Ahrens's *Sammlung chem. und chem.-techn. Vorträge* IV. 256 (Stuttgart, 1899)] Traube anticipated several points contained in his paper of 1901, and in my work in the same year, but this pamphlet was wholly unknown to me at the time. The fabric of Traube's reasoning is complicated by his hypothetical assumptions of 'Covolumen' and 'Kernvolumen,' 'gebundener' and 'freier Aether'; but nevertheless he deserves the credit of having appreciated the importance of many of the facts. The question of priority is of little consequence, especially since Müller-Erzbach (1881) had priority over both.''[33]

Traube naturally welcomed independent support, for views similar to his own, from such an eminent and influential chemist as Richards. It is obvious, from Richards's acknowledgment, that he found Traube's views about covolumes rather puzzling, as did most of their contemporaries. Richards and Traube fully agreed in the view that atoms were compressible.

Traube expanded his conceptions further by proposing that it was necessary to consider three categories of molecular volumes. (1) The "inner volume" of the atoms (*Kernvolumen*), the measure of which is the molar refractivity, R:

$$R = \frac{m}{d} \frac{n^2 - 1}{n^2 + 2}$$

where n is the refractive index; this volume is compressible. (2) The "external volume," which he defined as the space occupied by matter as such, increased by a shell of "bound ether," into which (according to Clausius) no other atom can penetrate. The measure of this volume is the b term of van der Waals. (3) The covolume, which he defines as the space required for the continual motion (*fortschreitende Bewegung*) of atoms and molecules. It is valid (Traube believed, as already indicated) for the liquid and solid as well as the gaseous state and is alterable with pressure and temperature according to the van der Waals equation.

Traube proceeded to interpret many physical properties of matter—hardness, elasticity, compressibility, thermal expansion, diffusion, viscosity, melting points, heats of combustion and vaporization, specific heat, and other properties—in the light of these concepts.[34]

He held the view that a more rational system of the chemical elements could be achieved by considering atomic volumes as of primary importance, rather than atomic weights. At that time there were still difficulties in the periodic system of the elements as formulated by Mendeleef and Lothar Meyer. The order of atomic weights was not always in harmony with the order that appeared rational in the light of the general properties of related elements—cobalt and nickel, for instance, were out of order, as were tellurium and iodine. A few year later these discrepancies were resolved by the work of Rutherford, Bohr, and Moseley, which demonstrated that atomic number, not atomic weight, was fundamental. In the context of his time, however, Traube could marshal some impressive arguments for his view. Necessarily such a view was complex; he could not classify the elements by assigning any single number to each, for he himself emphasized that atomic volumes were variables, not constants; but the very complexity of the data concerning atomic volumes could emphasize multiple subtle relations that might not otherwise be perceived. This particular line of thought has vanished, being

swept aside by the immense discoveries and new perspectives that emerged only a few years later; but it remains significant for those concerned with the history of scientific ideas.[35]

Volume Changes on Ion Formation: The Electrostriction Hypothesis and Traube's Critique

In 1894 Drude and Nernst pointed out that the electric field around an ion, immersed in a dielectric medium, would cause the medium to pack more compactly around the ion, if such close packing would increase the dielectric constant of the medium. The contraction would increase as the dielectric constant diminished, and would be greater for highly compressible solvents. They noted that the ionization of acetic acid and chloroacetic acid involved a decrease in volume of the order of -11 cm^3/mole, and the ionization of water involved a decrease nearly twice as great as this. This, they held, could be explained by the electrostriction effect. This work is of interest as being one of the earliest studies in which the effect of the electrostatic field of the ions on the surrounding medium was explicitly considered.[36]

Traube was unwilling to accept this explanation. His work had shown clearly that the transfer of *uncharged* organic molecules, from the pure organic liquid state to dilute aqueous solution, involved a substantial volume contraction, which could be as large as 12–13 cm^3/mole for non-associated liquids. (This corresponds to the difference between the two covolumes Φ, and ϕ, which we have already discussed). He interpreted this as representing an interaction, involving a volume decrease, between the solute and the water. This was of much the same magnitude as the decrease on ionization of acetic acid and other acids. He therefore postulated that every added solute particle, when dissolved in water, gave rise to such a volume contraction, whether the solute was an ion

or a neutral molecule. When a compound such as acetic acid ionized, he said, a single uncharged molecule gave rise to two ions. It was this increase in the number of solute particles, he believed, not the fact that the products of the dissociation were charged ions, that was significant in producing a volume contraction.[37]

Traube's explanation of the contraction was plausible and appeared to fit the existing facts. Perhaps the most definite test of the electrostriction hypothesis came about forty years later, from studies on amino acids. I must note that in this matter I am not a detached historian, since I was a member of the group that did the amino acid work, in the laboratory of Physical Chemistry at Harvard Medical School headed by Edwin J. Cohn. This work arose from the fundamental studies of E. Q. Adams and of N. Bjerrum who had concluded that the aliphatic amino acids must exist, when electrically neutral, primarily—indeed almost entirely—in the form of dipolar ions (Zwitterionen) with the formula $^+H_3N \cdot CH(R) \cdot COO^-$, rather than as isomeric uncharged molecules $H_2N \cdot CH(R) \cdot COOH$.[38]

This led Cohn, and his younger associates, of whom I was one, to an extensive study of various properties of amino acids and related compounds in the light of this postulated structure. In our studies on volumes it was soon apparent that the molecular solution volume (apparent molar volume) of an amino acid was substantially smaller than that of isomeric substances that did not carry such charged groups.

Thus for example the simplest amino acid, glycine, if its structure corresponded to the earlier accepted formula, $H_2N \cdot CH_2 \cdot COOH$, $(C_2H_5O_2N)$ should give by summation of Traube's atomic volumes in Table II, a value of $\Sigma V_a = 42.9$ cm^3/mole. Adding 12.4 for the covolume would give an expected v_m of 55.3 cm^3/mole. This is close to the observed value for an isomer of glycine, glycolamide $(CH_2OH \cdot CONH_2)$ which is 56.2; but the

value for glycine itself is only 43.5. The observed glycine value happens to be very close to ΣV_a, but this is accidental, as can be seen by comparison with other pairs of isomers in Table III. The uncharged compounds all have v_m values very close to those calculated by Traube's procedure. The amino acids, including the peptide glycylglycine, which carry simultaneously positive and negative ionic groups, all have markedly lower v_m values than their uncharged isomers. There is no question here of dissociation into different numbers of particles, as there is with the ionization of acids. The differences between the isomers must therefore be due to an electrostriction effect, as proposed by Drude and Nernst. The values (E) of this effect, as seen in the last column of Table III, increase with the separation between the positive and negative charges, as would be expected since the packing of water dipoles around the charges proceeds with less mutual interference if the charges are far apart.[39] Thus these studies on amino acids appeared to provide full confirmation of the electro-

striction hypothesis. Traube, who had done more than any other one person to correlate molecular volumes with structure, was wrong on this particular issue. His views on this matter were interwoven with his controversial interpretation of the ionization theory of Arrhenius, to which we turn next.

THE IONIZATION OF ELECTROLYTES: TRAUBE AS AN AMBIVALENT CRITIC OF ARRHENIUS AND VAN'T HOFF

In 1883, as a young man of 23 in Heidelberg, Traube had been studying the work of Raoult, Wüllner and other authors on the vapor pressure of aqueous solutions of electrolytes and nonelectrolytes. This inspired him, early in 1884, to compose a manuscript "Über die Beziehungen einiger für Lösungen und Gase annährend geltenden Gesetze." The manuscript apparently does not survive; we have only Traube's summary in his memoirs: "Like numbers of molecules of diverse substances, dissolved in a constant amount of water, diminish the vapor tension

TABLE III

Apparent Molar Volumes (v_m) of Dipolar Ions and Their Uncharged Isomers at 25°C
(E denotes the difference in each case between charged and uncharged isomers)

Substance	v_m (Traube)	v_m (obs)	E
Glycolamide ($CH_2OH \cdot CONH_2$)	57.2	56.2	
Glycine ($^+H_3N \cdot CH_2 \cdot COO^-$)		43.5	12.7
Lactamide ($CH_3CHOH \cdot CONH_2$)	73.5	73.8	
α-Alanine ($^+H_3N \cdot CH(CH_3)COO^-$)		60.6	13.2
β-Alanine ($^+H_3N \cdot CH_2 \cdot CH_2 \cdot COO^-$)		58.9	14.9
Methylhydantoic Acid ($H_2N \cdot CONH \cdot CH(CH_3)COOH$)	90.0	94.2	
Glycylglycine ($^+H_3N \cdot CH_2 \cdot CONH \cdot CH_2COOH^-$)		77.2	17.0

All values are in cm³/mol. The values in the v_m (Traube) column are calculated from Traube's atomic volumes, listed in Table II, except that the value for a CH_2 group is taken as 16.3 at 25°, instead of 16.1 at 15°C. The covolume is taken as 12.4 cm³/mole. The electrostriction, E, is given by the observed difference in v_m between a dipolar ion and its uncharged isomer. This involves the assumption that the volume contribution of a nitrogen atom (1.5 cm³/mole) is the same whether the nitrogen is trivalent or is quadricovalent and positively charged. This is in contradiction to Traube's assumption (Table II) that the latter form of nitrogen makes a much larger contribution to the volume than trivalent nitrogen does. If Traube's values were used here, the calculated electrostriction values would be larger than listed here, by 9.2 cm³/mole. This seems improbable.

This Table is based on work of T. L. McMeekin *et al.* and is taken, with some modification, from Cohn and Edsall (see note 19), p. 158.

of water, and diminish the temperature of maximum density, to the same extent. I pointed out the analogy with the laws of Boyle, Gay Lussac, and Avogadro.

"Raoult had determined that the molecular lowering of the freezing point for many substances was twice as great as for many others, but he avoided adopting such a hypothesis as that of Arrhenius to explain these facts. Raoult pointed out that these molecular numbers stood in integral ratios, $n:m$. He was however inclined to set $n = m$, and to assume that the observed anomalies were perhaps to be attributed to an association of the molecules. The molecular lowerings of the freezing point behaved *as if* one might conclude that a salt like KCl was dissociated into its ions. [He added a quotation from Raoult, which in English translation reads]:

But to infer from this a *real separation* of the ions, when they are dissolved, would be, to my mind, scarcely logical. I would maintain what I have said before: salts dissolved in water are in a special state in which the ions, despite the fact that they are combined, nevertheless act on the solvent so as to produce the same physical effects as if they were free ions.[40]

"One may see at once," writes Traube, "that there is a difference between the assumptions of Raoult–Traube and the later assumptions of van't Hoff–Arrhenius". However there is clearly a close relation between the two in the application of the gas laws to solutions.

Traube had some hesitation about submitting his manuscript for publication, and sent it for advice to Lothar Meyer, whose book, *Die Modernen Theorien der Chemie*, had greatly impressed him. Meyer replied at length on 11 March 1884, in a letter that Traube gives in full. The main point of his advice was for Traube to lay the manuscript aside for a year or two, to devote himself to experimental work. He admitted that, as a young man, he had not followed his own advice, but had published some purely

theoretical papers, when theories were in a state of great confusion. In his words "there was a veritable Augean Stable of Theories in those days." Now (1884), he said, things are different: we need solid experimental studies, on sound foundations, in which such variables as time, temperature, and masses of components are well defined. He advised Traube to strengthen his knowledge of mathematics, which would be of vital importance in years to come. There was an implication that Meyer had misgivings about the trustworthiness of Raoult's experimental work, though he did not state this explicitly.

Traube followed Meyer's advice, and did not publish, but it is not surprising that his feelings were mixed. On the one hand he remarked: "This did no harm, for a few years later van't Hoff did it much better than I."[41] Yet clearly he had a sense of lasting regret, which led him, nearly fifty years later, to send a copy of that early manuscript, with some description of its history, to the eminent chemist Paul Walden in Rostock. Walden replied two weeks later (11 November 1932) with a gracious and quite charming letter, expressing regret that Meyer had dissuaded Traube from publishing the article. The best new theories, he said, often arise in young minds that are not oppressed by a great mass of experimental material, or inhibited by the dignity of an established position. He mentioned Robert Mayer's ideas on energy, and van't Hoff's conception of the tetrahedral carbon atom, as examples, and expressed regret that the 24-year-old Traube had not gone ahead to publish his ideas.

The date of this letter is worth noting. Within three months Hitler would be Chancellor of Germany, and in less than a year after that Traube would leave Germany, never to return.[42]

We return to the early days of physical chemistry, and the publication of the epoch-making papers of van't Hoff and Arrhenius in the first volume of the *Zeitschrift für Phy-*

sikalische Chemie.[43] Their subject matter was the same as that of Traube's unpublished paper, but it was undoubtedly developed much more fully and adequately than Traube would have done it. In any case Traube, though profoundly impressed by their work, differed strongly with some of their fundamental conceptions. Van't Hoff, drawing largely on the osmotic pressure studies of the botanist W. Pfeffer, showed that the osmotic pressure (II) of dilute aqueous solutions was given to a very good approximation by the limiting equation

$$\Pi = RTm = RTn/V \qquad (11)$$

where n is the number of moles of solute in volume V, which corresponds to the perfect gas law, writing II instead of the gas pressure P. He showed also the intimate thermodynamic relation of osmotic pressure with the lowering of solvent vapor pressure and with the freezing point depression. He emphasized the analogy of gas pressure with osmotic pressure.

In the first case it is due to the impacts of the gas molecules on the containing walls, in the second to the impacts of the dissolved molecules on the semipermeable membrane. The molecules of the solvent present on both sides of the membrane, since they pass freely through it, need not be taken into consideration.[44]

This statement raised a conceptual difficulty that Lothar Meyer soon pointed out. A gas inside a container exerts an outward pressure due to the bombardment of the container walls by the gas molecules inside; but when a solution is confined inside a semipermeable membrane, with pure solvent outside, the spontaneous direction of solvent flow is *into* the solution. A pressure, the osmotic pressure, has to be applied to the *inner* solution to keep solvent from flowing in. Numerically van't Hoff's equation appears to fit the facts, but it has the wrong sign.

Van't Hoff, replying to his "greatly honored critic" (mein hochvehrerter Gegner)

proposed a conceptual experiment. Consider a semipermeable membrane, permeable to hydrogen but impermeable to nitrogen, with nitrogen confined inside. Now add hydrogen outside; it will pass through the membrane until the hydrogen pressure is equal on both sides, though the total pressure is greater on the inside. Then surely we must attribute this excess pressure to the nitrogen. Now imagine the hydrogen pressure to increase until it becomes a liquid. The nitrogen on the inside is now the dilute solute, dissolved in a great excess of hydrogen; yet since it is the hydrogen that is in equilibrium between the two sides, it must still be the nitrogen on the inside that is responsible for the excess pressure. In any case, said van't Hoff, however we look at this argument, the limiting equation is soundly based on thermodynamic grounds. Although this was indeed true, it took years to formulate the thermodynamic argument in a way that was readily understandable and convincing to most chemists.[45]

Traube's criticism of the views of van't Hoff and Arrhenius arose primarily from his conviction that the analogy between solutions and gases neglected the basic fact of interaction between the solute and the solvent. Moreover the conception that such a solid crystal as rock salt, on dissolving in water, would break up into charged ions that could wander freely and independently through the solution, affronted his notions of what was chemically reasonable. That was his foremost reason for questioning the scheme of Arrhenius, in a paper that appeared in 1890. He also listed fourteen other queries and objections, involving diffusion, freezing point data, colors of salts, heats of "dissociation" and other items. He emphasized correctly that the Ostwald dilution law held only for weak electrolytes, but many of his points seem today somewhat obscure and confused. Ostwald in his journal wrote a caustic *Referat* of Traube's paper: "Misunderstood marginal notes on the theory of Arrhenius, which deserve no further discus-

sion." Arrhenius replied, however, in two papers in the *Berichte* (1891). In the second of these he pointed out some serious errors in Traube's measurements of the freezing points of sucrose (cane sugar) solutions, which Traube had used to bolster some of his arguments. Traube's data were in contradiction to those from four other laboratories, including those of Arrhenius and van't Hoff, which all agreed well among themselves. Plainly Traube's data were in error, and he appears at his weakest in this particular controversy.

In 1892 Traube clarified his views by drawing a fairly sharp distinction between the concept of ionization, which he accepted, and that of dissociation. It was the idea of ions as freely dissociated particles, which could wander separately through the solution, that he could not accept. Instead he pictured the ions of a salt, in solution, as still coupled to one another by electrical attraction, as if they were tethered on a leash that allowed them to move apart a little way, but not to wander independently, except by exchange with other neighboring ions. The association of ions with water molecules was also an essential part of his picture. In some writings he saw this as an attachment of one water molecule per ion, sometimes with more water than that. An undissociated molecule of salt, he postulated, should also have at least two associated water molecules.[46]

Traube received support for his criticisms of Arrhenius from two well-known physicists. J. H. Poynting of Birmingham wrote to him: "As to the case of an electrolyte I have no objection to urge against the dissociation of NaCl, provided that the Na and the Cl are not free but separately combined with the H_2O molecules." Traube agreed, and welcomed Poynting's support. G. F. Fitzgerald wrote from Dublin:

For me you seem to hold quite sound views and I regret that, at the time I wrote the Helmholtz Memorial Lecture, I was unable to discover the law of contraction you have demonstrated. . . . I am very glad that German scientific men are taking up that position, that the part played by the solvent must not be left out of account. I am the better pleased at it because it is very unfortunate if scientific questions get into the condition of being called "The English view" and "The German view."

Traube was clearly comforted by this kind of support from distinguished colleagues abroad, in his rather lonely stand against the prevailing views among his contemporaries in Germany.[47]

Traube published a textbook *Grundriss der Physikalischen Chemie* in 1904. In this he dealt with electrolytic dissociation in two stages; first presenting the theory from the point of view of Arrhenius, as Traube understood him, then following with five pages, presenting his own interpretation of the data. He emphasized that the mass action law was valid only for weak electrolytes, and for the role of solvent-solute interaction and binding he again coupled his views with those of Poynting. He also emphasized the evidence for the interaction of ions with solvent molecules from the volume contraction on mixing solvent and solute, which had played so large a role in his work on molecular volumes.[48]

Central in Traube's thinking about solutions was the concept that he termed *Haftdruck*; in one of his papers, published in English, in 1910, this was translated as "attraction pressure," in another as "cohesion pressure." In the former paper he writes that the *attraction pressure* is "the cohesion constant a_{12} of van der Waals. The *attraction pressure* is the *intensity factor* of the solution energy and has been neglected in the theories by van't Hoff and Arrhenius.

If for example we dissolve in water a substance like sugar or alcohol, we change the energy content of the system to a certain extent. This change is proportional, firstly, to the number of the dissolved particles—that is a capacity factor—and

proportional secondly to an intensity factor "the attraction pressure," that is the pressure which corresponds to the union of the substance and the solvent.

There is scarcely a single physical or physiological property of the solutions, which is not intimately connected with the attraction pressure.

He then sets forth the role of the attraction pressure in determining the properties of solutions. For ions he gives a long list of such properties, including surface tension, compressibility, effect on solubility of proteins and nonelectrolytes, diffusion coefficients, molecular volumes, heats of solution, and various others. For each property he gives a rank order of the principal cations and anions, an order generally much the same for the different listed properties but differing somewhat from one to another. He gives a similar but somewhat shorter discussion of various properties of nonelectrolytes, emphasizing the physiological role of attraction pressure, for by this time his interests largely centered on physiology and physical biochemistry. Nowhere, however, does he give any quantitative estimate of the magnitude of the attraction pressure, nor indeed any indication of how such quantitative data might be obtained. The concept of *Haftdruck,* however, permeates his thinking throughout the rest of his career, and he constantly returns to it in his biochemical and colloidal studies.[49]

Many years later, in 1933, not long before he was to say farewell to Germany, Traube looked back on the progress of the theory of solutions, especially electrolyte solutions, which had achieved such great advances in quantitative understanding, through the work of Niels Bjerrum and others, culminating in the interionic attraction theory of Debye and Hückel. He wrote, in *Kolloid-Beihefte,* an extensive review hailing the new advances, and reviewing his long years as a critic of the limitations of the theories of Arrhenius and van't Hoff. Primarily this was a backward look over the development of his own ideas and the resistance he encountered in many quarters. He traced his concept of *Haftdruck*—or *Haftintensität,* as he later preferred to call it—through its development over nearly thirty years, and its application to surface tension, osmotic phenomena, electrical potential, and other properties, including its biological significance for such problems as permeability and narcosis. At the end he remarked that his critics pointed out that the *Haftdruck* theory had only a qualitative character, but he held that the work of W. B. Hardy, W. D. Harkins, and others pointed the way toward determining the *Haftintensität* (or work of adhesion) in surface films; and there were other promising approaches also.

Wolfgang Ostwald, the Editor of *Kolloid-Beihefte* (and son of Wilhelm Ostwald) appended a short editorial comment on Traube's review. Some of his comments deserve quotation:

The undersigned (and probably also many other readers) cannot subscribe without qualification to all the author's views, especially in the criticisms he has offered regarding the historical development of the field.

The service of I. Traube, in persistently calling attention to inadequacies in the classical theories, is indisputable. The view that not only the number of particles, but also the forces between them, of varying nature and magnitude, must be responsible for the behavior of a solution (or indeed for a disperse system)—this now represents the outlook of many researchers, and in a historical presentation of these considerations the name of I. Traube must stand in the front rank. But in the synthetic part of the author's researches, in the so-called *Haftdrucktheorie,* the undersigned cannot see a quantitative solution of the inadequacies of the older theory, but only a preliminary phenomenological formulation of the problem. And one cannot say that the newer theory of electrolytes, by Debye and Hückel and other investigators, in which the forces between the particles play an essential role, is a consequence of the objections [to the older theory] that I. Traube has raised for decades past.[50]

Traube looked upon himself as a forerunner of the advances in the quantitative theory of electrolytes that culminated in the work of Debye and Hückel; but they, and such investigators as G. N. Lewis and Niels Bjerrum, did their work with a background in physics and mathematics, which Traube did not possess. He was a largely forgotten prophet, for the leaders of the new age were working in realms of thought where he could not follow. As Wolfenden has remarked: ". . . The anomaly of strong electrolytes was a problem which only physicists could solve and in whose solution only chemists were interested."[51] Traube came nowhere near solving the problem, but neither did any of his contemporaries, some of whom were much better equipped with knowledge of mathematics and physics. It grieved him that his efforts had been forgotten by the chemists of the younger generation, but that was a fate that he has shared with others.[52]

TRAUBE'S CONTRIBUTIONS TO
BIOCHEMISTRY, PHARMACOLOGY,
MEDICINAL CHEMISTRY AND
COLLOID CHEMISTRY

In 1900 Traube received the title of Professor (*extraordinarius*) at the Technische Hochschule in Berlin, but his situation was evidently difficult. He never became Professor *ordinarius* in spite of achievements in research for which (as he put it) many "Ordinarien" could have envied him. He considered his treatment by certain influential persons as involving humiliations (Demütigungen), and concluded that, as a matter of necessity, he must turn the direction of his research from general physical chemistry to colloid chemistry.[53]

However, even though this shift of interests may have occurred under the influence of external pressure, Traube pursued research in this new area with his accustomed intensity and energy. By his own account he lacked technical assistants and adequate laboratory equipment, and had relatively few well-trained students to work with him.

There was, however, an enduring continuity in his intellectual outlook. His early work on surface tensions of organic compounds in water, and on the tendency of compounds containing nonpolar groups to concentrate at interfaces, was central to his thinking about such biological phenomena as cell permeability, narcosis, toxicology, and the action of drugs. Also the concept of *Haftdruck*, which we have already discussed, was one to which he constantly returned.

What factors determined the permeability of living cells to certain substances, and their impermeability to others? Before 1890 there had been important observations on a few substances, such as urea and glycerol, by K. Klebs and by Hugo de Vries, later famous for his work in genetics. During the following decade a young man, (Charles) Ernest Overton (1865–1933) transformed the field. Overton, son of an English clergyman, lived in England until 1882, when his mother moved to Switzerland for her health, taking her children with her. Overton obtained his doctorate in botany in 1889 at the University of Zürich, where he remained until 1901, a period in which he did his most creative work. Then he moved to Würzburg, Germany, until 1907, when he became Professor of Pharmacology at the University of Lund in Sweden.

Studying the rate of penetration of more than 200 organic and inorganic substances into various plant and animal cells, Overton found a systematic correlation between their penetration into cells and their tendency to dissolve in fatty solvents (such as olive oil) rather than in water. There were, of course, some variations between different types of cells. In general, however, the correlation appeared good. The most notable exception to the rule was water itself. Its ready entry into cells had to be explained on other grounds, such as the small size of the water molecules. In general, however the lipid (or

lipoid) solubility theory served well to correlate a large body of experimental facts. (The term used in Overton's day was lipoid, for this class of substances; later, around 1930, it was officially changed to lipid). Overton suggested that cholesterol and lecithin, or closely similar substances, might play an important role in the membrane structure, thereby favoring the transport of fat-soluble substances across the membrane.

Overton also noted that many of the substances that readily penetrated the cell also possessed narcotic action; permeability and narcosis were closely, though not invariably, related. He developed these ideas in detail in a short monograph (1901)—the only book he ever wrote. Independently the distinguished pharmacologist Hans Horst Meyer (1853–1939) in Marburg (later in Vienna) developed views, concerning narcosis, almost identical with those of Overton, though on a less extensive experimental basis. Their concepts were often referred to as the Meyer–Overton theory of narcotic action.

Traube, while expressing great admiration for the contributions of Overton and Meyer, held that the tendency of a substance to lower surface tension was more fundamentally correlated with cell permeability and narcotic action, than was its solubility in fatty solvents. "Surface active" compounds would tend to accumulate at an interface, such as a membrane separating the cytoplasm of a cell from the liquid phase outside. Their actual passage through the membrane of course depended fundamentally on the nature of the membrane itself, but here also there was a high correlation between rate of passage and either lipid solubility or surface activity. For Traube the correlation with the latter property appeared closer and more fundamentally based than with the former, and he argued his point of view vigorously and repeatedly from the time when he first enunciated it in 1904.[55]

Traube believed that most contemporary physiologists, pharmacologists, and immu-

nologists laid too much stress on the chemical structure of the compounds they were studying, and paid too little attention to the physical chemistry of the systems involved. He thus considered that Paul Ehrlich, with his sidechain theory of immunological processes, held a limited and one-sided view, and he noted with pleasure that such an eminent pharmacologist as Hans Horst Meyer became in time more sympathetic to the physico-chemical view advocated by Traube.[56]

Traube wrote many papers on the mechanism of narcosis. He regarded narcotics as substances that inhibited cellular activity, notably oxidative and especially electrical activity. In a paper with P. Klein he stressed the importance of the state of dispersity of many narcotics as a determinant of their activity or inactivity. Making use of the ultramicroscope and of light-scattering measurements, Traube and Klein found that many hydrocarbons, also halogen alkyl derivatives, and such substances as amyl alcohol and aniline, were present, in aqueous solution, at least in part, in a colloidal state in which they lacked narcotic activity, whereas they were active in molecular dispersion. It was observations of this sort that led Traube to the view that pharmacological activity was largely dependent on physical conditions, and that these had been neglected by those who emphasized only chemical specificity.[57]

Traube seems to have had difficulty in converting others to his views on permeability and narcosis. Surface activity and solubility of substances in fatty solvents were highly correlated. Thus, to many investigators, it was difficult to see any clear basis of distinction between Traube's theory and that of Overton and Meyer. It would appear that most others did not consider Traube's views to be wrong; rather they thought that he was merely translating the lipid solubility theory into a different language. This appears, for instance, to have been the attitude of Rudolf

Höber, author of the widely influential textbook *Physikalische Chemie der Zelle und der Gewebe.* Höber remarked, in one article, on the "flood of papers" in which Traube was trying to persuade others to use a different language in describing the phenomena of permeability and narcosis. Traube replied that he still hoped to persuade Höber of the correctness of his views, even if another flood of papers might be required to do it.

In a later edition of his textbook (1922–24) Höber gave a comprehensive discussion of problems of permeability and of narcosis. In these two long chapters, he brought out clearly the complexity of the experimental data, which could not all be fitted into any simple theory. On the whole Höber tended to favor the views of Overton and Meyer, rather than those of Traube, but he did discuss Traube's views in considerable detail, and treated them with respect. Höber recognized the importance of Traube's work on surface tensions, which he discussed in an earlier chapter. In contrast, we may note that W. M. Bayliss in London, in his great and influential treatise *Principles of General Physiology,* did not include any of Traube's work in his bibliography, but did refer extensively to Overton and also to Meyer.[58]

At least one outstanding investigator, Otto Warburg, held Traube's theory to represent a real advance on that of Overton and Meyer. In a study of the oxidation of oxalic acid on blood charcoal (1914) Warburg wrote: "We know today that, under the influence of narcotics, the ferments [in the living cell] are precipitated or that their active surface is diminished. We know further that narcotics are concentrated in those regions of the cell where combustion takes place, upon which in all probability the major action of narcotics on ferment reactions in the cell depends. We know finally, at least for some narcotics, that they become concentrated [in such places] even after the lipids have been removed. All these facts, which can be explained on the lipid theory only by assumption of further

hypotheses, are readily explained on the basis of Traube's point of view." Later, in 1928, in a survey of the field, Warburg cited Traube's work on surface tension of aqueous solutions as one of the essential foundations of the theory of narcosis.[59]

In one of his last papers on narcosis, Traube gave a broad view of the subject as it was then understood, modifying some of his earlier views and taking account of the views of his critics, though still holding to his general point of view. In the same year (1928) he published, with F. Dannenberg, a critical review of the permeability problem, in which they also reported new experimental work. Dealing with various theories that had been proposed, they rejected the simple concept of membranes as sieves that let through small molecules and hold back larger ones; a view which they ascribed to Moritz Traube, Collander, Ruhland, and L. Michaelis. Concerning permeability to ions, they recognized that the state of charge in the membrane could be crucial in determining the possible passage of ions; only ions with the opposite sign of charge could pass through, and there might be further restrictions even on these. They emphasized the different properties of various types of membranes. With collodion membranes, for instance, they found that amyl alcohol penetrates less readily than ethanol, in contradiction to Traube's general correlation of penetrating power with surface activity. Thus, though the "surface activity" theory had led to valuable new insights, they acknowledged that it was not a truly general theory, and that such a theory must be quite complicated.[60]

Traube studied also the action of toxins, immunological phenomena, and the growth of plant cells and cancer cells. In all cases he stressed the great importance of surface forces, and in the attempt to explain immunological specificity on a physical basis he developed a "resonance" theory of antigen-antibody interaction. As far as I know,

the latter theory had little influence among the immunologists. In the study of cancer he again emphasized the role of surface-active compounds in the organism, citing also the work of certain Russian investigators (Kagan, Soloviev) who found, in accord with Traube's views, that lowering of surface tension tended to run parallel with increased rate of growth of tumors. Traube, in later work with Dr. Else Knake, reported that the balance in growth of tissues between the development of epithelium and that of connective tissue was altered by factors that increase cell permeability. Dr. Knake found that various alcohols, fatty acids, amines, and other surface-active compounds promote the development of epithelium relative to connective tissue, and that this effect ran parallel to the lowering of surface tension in the compounds in question. Although Traube's work on cancer appears to have been largely forgotten in later years, he was elected in 1925 as a fellow of the German Central Committee for Research and Prevention of Cancer (Deutsches Zentralkomitee zur Erforschung und Bekämpfung der Krebskrankheit); an honor that he greatly valued.[61]

His activities ranged over many subjects that can only be mentioned here, such as his technical researches on the purification of tobacco, which led to patents in most countries of the world. These processes served both to remove much of the nicotine and to improve the smoking quality of the tobacco. Traube served for many years as head of the company that employed the process commercially in Germany, until the Nazis came to power and removed him. Traube also was active, during the First World War and afterwards, in the development of synthetic rubber and rubber substitutes, in work on the stabilization of foams and emulsions, and in diverse other activities.[62]

TRAUBE AS EDITOR OF AN INTERNATIONAL JOURNAL

Traube envisaged, organized and edited an international journal of physico-chemical biology which in happier times might have flourished and been widely influential. He enlisted the support and cooperation of three eminent associate editors, Jacques Loeb in New York, Victor Henri in Paris, and H. J. Hamburger in Groningen. Associated members of the editorial board of about fifty included such scientists as W. M. Bayliss (London), G. Bertrand (Paris), J. Bordet (Brussels), F. Bottazzi (Naples), H. von Euler (Stockholm), O. von Fürth (Vienna), E. N. Harvey (Princeton), L. J. Henderson (Cambridge, Mass.), K. Landsteiner (Vienna), A. B. Macallum (Toronto), T. Madsen (Copenhagen), Sven Oden (Uppsala), W. J. V. Osterhout (Cambridge, Mass.), W. Pauli (Vienna), T. B. Robertson (Berkeley), P. Rona (Berlin), S. P. L. Sørensen (Copenhagen) and others; a very distinguished list by any standards.

Traube's preface to the opening issue of the *Internationale Zeitschrift für Physikalisch-Chemische Biologie* recalled the great impact on the world of science of the founding of the *Zeitschrift für Physikalische Chemie* in 1887, and emphasized that the time appeared ripe for a similar journal devoted to the role of physical chemistry in biology. This opening issue contained a truly international collection of papers; from the United States there were papers by E. N. Harvey, J. F. McClendon and others; from Denmark the great August Krogh had a contribution. There were of course papers from Traube himself.

Traube could not know that he had launched the journal at the worst possible moment; this issue appeared in April 1914. Within four months Europe was engulfed in war. The spirit of international cooperation, which had been so strong in the pre-war years, was profoundly shaken and torn. Communication inevitably became difficult. The journal indeed did continue publication through several volumes, with its authorship increasingly confined to Germany and its allied neighbors. Finally, about the end of the war, it ceased publication—a casualty of the war.[63]

TRAUBE'S PLACE IN THE SCIENCE
OF HIS TIME

Except for the perpetuation of his name in "Traube's rule," Traube remains a largely forgotten figure today. This fate seems undeserved. His experimental work on surface tensions of aqueous solutions of organic compounds was of outstanding range and quality; he grasped many of its implications, and set forth his conclusions with clarity in his major paper in 1891. It was not until more than a quarter of a century later that Irving Langmuir perceived the far-reaching significance of Traube's work, in the course of his own great advances in the understanding of surface chemistry. Traube's work on molecular volumes of pure liquids, and especially on the apparent molar volumes of dissolved molecules in water and other solvents, was also a major contribution, and clearly influenced others. Sir William Ramsay wrote to him, 17 March 1897: "Recently I have read all your papers on specific volumes, and I cannot fail to tell you of my great admiration for the beautiful relations which you have derived from this work. It is really splendid that you have thrown light on such complicated problems, and I heartily congratulate you." Ramsay went on to say that Traube's work would greatly enhance the interest of studies on the compressibility of solutions that were going on in his own laboratory.[64] I have already noted the relation of Traube's work on molecular volumes to that of Theodore Richards, and his influence on the work at Harvard Medical School, in the laboratory headed by E. J. Cohn, in the 1930s. Traube's interpretation of molecular covolumes, and his extension of the van der Waals equation to liquids and solids, remain stimulating and imaginative ideas that may yet exert future influence.

His criticism of the views of van't Hoff and Arrhenius, on the nature of solutions and the phenomenon of ionization, was based primarily on what he considered their neglect of solvent-solute interactions. Nevertheless he considered their work to represent the greatest advance in physical chemistry during the last two decades of the nineteenth century, and indeed he had anticipated some of their conclusions in his early unpublished manuscript of 1883. His criticisms of their views look somewhat confused to the eyes of a modern reader, but his confusion was shared by various distinguished contemporaries. He suffered because of these criticisms; Willhelm Ostwald did not accept any of his papers in the *Zeitschrift für Physikalische Chemie*, and he was generally looked upon as an odd character by his contemporaries and juniors in physical chemistry in Germany.

His later contributions to biochemistry, pharmacology, immunology, and colloid chemistry are more difficult to appraise. His earlier work on surface forces profoundly influenced his outlook on work in these areas, and with good reason. His emphasis on physical, rather than primarily chemical, interpretations of biological specificity was characteristic of many of his contemporaries in colloid science and related fields. Later work showed that the role of chemical specificity was much greater than they had recognized. Traube reinterpreted the permeability theories of Ernest Overton and H. H. Meyer, while expressing profound admiration for their achievements. His addiction to controversy was characteristic, and involved his personal dedication to the truth as he saw it; clearly no personal malice was involved in his disagreements with others, though his unceasing persistence in his criticisms must sometimes have been exasperating to those he criticized. He remains a rather lonely and certainly independent figure, whose achievements should not be forgotten.

ACKNOWLEDGMENTS

his publications. Copies of all this material have been deposited in the Edgar Fahs Smith Library, Center for the History of Chemistry, at the University of Pennsylvania, Philadelphia; and in the Library of the American Philosophical Society, also in Philadelphia. Dr. Boas-Traube has also given to the E. F. Smith Library a bound set of fourteen volumes of her father's papers, including his textbook of physical chemistry and the published volumes of the *Internationale Zeitschrift für physikalisch-chemische Biologie*. These materials proved of great value in the study of Traube's work. The late Sir Hans

Krebs, whose mother was a first cousin of Traube, brought me into touch with Dr. Boas-Traube, and gave me helpful information during the last months of his life. Dr. Boas-Traube, in a series of letters, has supplied additional personal information about her father.

I thank Joseph S. Fruton and Erwin N. Hiebert for reading the manuscript and offering helpful suggestions and corrections.

I am indebted to the National Science Foundation for a grant, SOC 7912543, which provided essential support for this work, especially in its earlier phases.

Notes

1. See for instance Charles Tanford, *The Hydrophobic Effect: Formation of Micelles and Biological Membranes*, Second Edition (New York: John Wiley and Sons, 1980), xi + 233 pp. Tanford's comments on Traube are on pages 2 and 3.

2. See R. G. A. Dolby, "Debates over the Theory of Solution: a Study of Dissent in the English-Speaking World in the late Nineteenth and Early Twentieth Centuries," *Historical Studies in the Physical Sciences* (R. McCormmach, editor) 7 (1976): 297–494. This valuable and comprehensive study does not mention Traube.

3. Traube wrote two autobiographies: a short one (11 typed pages) in 1930, entitled "50 Jahre Laboratoriumsarbeit" and a much longer one, "Lebenserinnerungen" (101 typed pages) in the last year of his life, 1942–43. In what follows, I cite the longer one by its title "Lebenserinnerungen" with page references; and the shorter one as "50 Jahre Arbeit." Neither of these has been published; I am indebted to Traube's daughter, Dr. Sonja Boas-Traube, now living in Windsor, England, for sending me the original copies, together with a comprehensive bibliography of her father's publications. Photocopies of all this material have been deposited in the library of the American Philosophical Society in Philadelphia, and in the Edgar Fahs Smith Library of the History of Chemistry at the University of Pennsylvania, also in Philadelphia. For further related comments see the Acknowledgments.

4. Concerning the beauty and character of the old city of Hildesheim, see for instance Hans Krebs, *Recollections and Reflections* (Oxford: Clarendon Press, 1981), especially pages 1–3. Krebs, whose mother was a first cousin of Traube, also grew up in Hildesheim. The old city was almost completely destroyed by bombing in the last year of the Second World War, and since rebuilt as a modern city. For my indebtedness to Sir Hans Krebs, see Acknowledgments.

5. "Lebenserinnerungen," p. 2.

6. Concerning Baumann, see for instance Albrecht Kossel, "Eugen Baumann, 1846–1896," *Zeitschrift für Physiologische Chemie* 23 (1897): 1–22. For other references on Baumann, including a recent book, see Joseph S. Fruton *A Bio-Bibliography for the History of the Biochemical Sciences since 1800* (1982) American Philosophical Society, Philadelphia, p. 43.

7. This account is drawn chiefly from the first 28 pages of the "Lebenserinnerungen," where he discusses his life and career, with interspersed accounts of his scientific work and ideas. The statement about his salary as *ausserordentlicher Professor* is from "50 Jahre Arbeit," 5. Concerning Dr. Guido Bodländer and his association with Traube, see note 24 below.

8. For three such articles see H. Freundlich, *Kolloid Zeitschrift* 50 (1930): 194–196; R. E. Liesegang, *Chemiker-Zeitung* 54 (1930): 249–251; L. J. Weber, *Zeitschrift für Angewandte Chemie* 43 (1930): 272–274.

9. In the "Lebenserinnerungen," Traube provides virtually no glimpses of his personal life beyond the age of 30; in all the later pages he concentrates on a survey of his work and his ideas, which he was obviously eager to set down in the closing months of his life. For information about his life in Scotland, and marriages and children, I am indebted to letters from Dr. Sonja Boas-Traube, especially one dated 12 January 1983. See also the obituary on Traube by D. H. Bangham, *Nature* 152 (1943): 743–744.

10. For his first paper on surface tension, see I. Traube "Capillaritätserscheinungen in Beziehung zur Constitution und zum Molekulargewicht," *Berichte der deutschen Chemischen Gesellschaft* 17 (1884): 2294–2317; also a related paper in *Journal für Praktische Chemie* (Neue Folge) 31 (1885): 177–218.

11. "Lebenserinnerungen," p. 15.

12. E. Duclaux, "Sur la tension superficielle dans la série des alcools et des acides gras," *Annales de chimie et de physique* 13 (1878 [5]): 76–101. Traube's first re-

searches in the field were done before he became aware of Duclaux's work; he added a footnote concerning Duclaux to a paper in 1886, and discussed Duclaux's work in more detail in his major paper of 1891 (see next footnote).

13. I. Traube, "Ueber die Capillaritätsconstanten organischer Stoffe in wässerigen Lösungen," Liebig's *Annalen der Chemie* 265 (1891): 27–55. In reading Traube's tables, one must remember that his symbol c denotes the *reciprocal* of the molar concentration of the solute, i.e. the dilution; and his symbol E denotes $\gamma^0 - \gamma$, where γ^0 is the surface tension of water and γ is that of the solution in question, with values in dyne cm^{-1}. The numerical values in the last column of each of the long tables of data, with the heading $c \cdot E - 10$, are thus values of $(\gamma^0 - \gamma)/m$, where m is the concentration of solute, in moles per liter. The absolute values of surface tension are listed in the column headed $rhs/2 = \alpha \cos \theta$. (Here r is the capillary radius, h is the rise of liquid in the capillary and s its density. The values in this column, however, must be multiplied by 10 to obtain surface tension in dyne cm^{-1}. The angle of contact θ (*Randwinkel*) of the liquid with the capillary wall is assumed equal to $0°$ ($\cos \theta = 1$) although Traube was careful to note that this assumption is by no means assured. See his footnote on p. 28, with references to his earlier papers. Nevertheless, in the light of all subsequent work, the assumption appears to have been justified.

Traube had perceived qualitatively the general relations involved in his later work, as early as 1885, as shown most clearly by the figure (Tafel II) attached to his paper "Über die Bestimmung der Capillaritätsconstanten einiger wässrigen und alkoholischen Lösungen durch Beobachtung der Steighöhen im capillaren Rohre," *Journal für praktische Chemie* (N.F) 31 (1885): 177–218. (Note however that Tafel II is placed, not in or near this paper, but opposite p. 272, at the end of that issue of the journal.) In this figure he plots the concentration data in volume percent of solute; a plot which, he later realized, obscured the quantitative relations that he later discovered.

14. Traube, "Über die Capillaritätsconstanten" (note 13) 47–49.

15. See Traube's table on p. 52 of his paper cited above.

16. Bohdan von Szyszkowski, "Experimentelle Studien über kapillare Eigenschaften der wässerigen Lösungen von Fettsäuren," *Zeitschrift für Physikalische Chemie* 64 (1908): 385–414.

17. Irving Langmuir, "The constitution and fundamental properties of solids and liquids. II. Liquids." *Journal of the American Chemical Society* 39 (1917): 1848–1906. For Langmuir's detailed discussion of Traube's work, with an extensive table based on Traube's data, see pages 1889–1895 inclusive.

18. Irving Langmuir, "Surface Chemistry," (Nobel Lecture) *Chemical Reviews* 13 (1933): 147–191. See p. 163 for the remarks cited. Also published in *General Electric Review* 18 (1935): 402.

19. Thomas L. McMeekin, Edwin J. Cohn and John H. Weare, "Studies in the Physical Chemistry of Amino Acids, Peptides and Related Substances. III. The Solubility of Derivatives of the Amino Acids in Alcohol-Water Mixtures," *Journal of the American Chemical Society* 57 (1935): 626–633. For a more comprehensive survey of this and related work, see E. J. Cohn and J. T. Edsall, "Proteins, Amino Acids and Peptides as Ions and Dipolar Ions" (Reinhold, New York 1943; reissued by Hafner, New York 1965) Chapter 9, especially pp. 205–212.

20. Sonja Boas-Traube and M. Volmer. "Über die Gültigkeit der TRAUBEschen Regel für die Grenzfläche flüssig/flüssig," *Zeitschrift für Physikalische Chemie* 178 (1937): 323–335.

21. For a classical paper on hydrophobic interactions see Walter Kauzmann, "Some Factors in the Interpretation of Protein Denaturation," *Advances in Protein Chemistry* 14 (1959): 1–63. For later reviews, see Felix Franks, "The Hydrophobic Interaction," in *Water: a Comprehensive Treatise* (F. Franks, editor) Vol. 4 pp 1–94 (Plenum Press, New York and London 1975). Also J. T. Edsall and H. A. McKenzie "Water and Proteins," *Advances in Biophysics* (Tokyo), 10 (1978): 137–208 and 16 (1983): 53–183, especially pp. 64–95 of the latter article.

22. It has been difficult for me to find out how much was known by 1887 about the action of concentrated salts in effecting such two-phase separations. Bodländer may have observed this in his own experiments, or he may simply have called to Traube's attention a phenomenon already known to others. Two reviews that I have consulted—Paul M. Gross, "The 'Salting-out' of Nonelectrolytes from Aqueous Solutions," *Chemical Reviews* 13 (1933): 91–101, and F. A. Long and W. F. McDevit, "Activity Coefficients of Nonelectrolyte Solutes in Aqueous Salt Solutions," *Chemical Reviews* 51 (1952): 119–169—cite as their earliest reference the work of J. Setschenow, Memoirs of the Imperial Academy of Sciences, St. Petersburg (7) 22, No. 6 (1875), which I have not seen. Setschenow's later paper, "Über die Konstitution der Salzlösungen auf Grund ihres Verhaltens zur Kohlensäure," *Zeitschr. Physik. Chem.* 4 (1889): 117–125, deals with the salting out of carbon dioxide, and his earlier papers apparently dealt also with solubility of gases in aqueous salt solutions. Otherwise the earliest reference to work in this field, in the reviews cited above, dates from 1899.

23. See "Lebenserinnerungen," 22–28.

24. Bodländer had been a pupil of the distinguished physiological chemist Moritz Traube, and later went back to work with him for a time after the ending of his partnership with Isidor Traube. Later he worked at the Mining Academy in Klausthal, then for some years in Nernst's laboratory in Göttingen, and finally became Professor of Chemistry in Braunschweig, where he died in 1904 at the age of 49. Though he was not an investigator of the first rank, he was clearly held in high esteem by his colleagues; see the obituaries by A. Coehn, *Berichte* 38 (1905): 4263–4290, by W. Nernst, *Zeitschr. für Elektrochemie* 11 (1905): 157–161 and by R. Abegg on p. 1 of the same volume. (So far as I am aware Moritz and Isidor Traube were not related.)

25. Kopp gave a comprehensive survey of his researches: "Über die molekular Volume von Flüssigkeiten," *Annalen der Chemie* 250 (1889): 1–117. For useful surveys of his life and work, see A. W. Hofmann, *Berichte* 25 (1892): 505–521, and T. E. Thorpe, *Journal of the Chemical Society* 63 (1893): 776–815. Kopp was also notable as a historian of chemistry; concerning this work as well as his chemical activity, see M. Speter, *Osiris* 5 (1938): 392–460.

26. For further discussion of apprent molar volumes, and partial molar volumes, see for instance G. N. Lewis and M. Randall, *Thermodynamics* (McGraw Hill, New York 1923), 33–40; or the revised version of this text by K. S. Pitzer and L. Brewer, 1961: pp. 205–210. Most of their discussion is devoted to the partial molar volume, which is the differential volume increment, per mole of solute added. For dilute solution, especially of nonelectrolytes, Traube's v_m is sufficiently close to $\partial V/\partial n$ that we can disregard the difference between the two in our discussion.

27. The existence of such a contraction was already well known. For instance Dolby, "Debates over the theory of solution" 301 (see note 2) cites the work of J. J. Griffin, *Philosophical Magazine* [3] 29 (1846): 289–310 and 444–467, who discussed this volume contraction in terms of internal pressure, and concluded that the increase of this pressure on mixing the liquids was so large that it implied chemical combination between the components.

28. Traube published numerous papers, from 1892 on, on his volume studies. His comprehensive review "Über den Raum der Atome" in *Sammlung chemischer und chemisch-technischer Vorträge* (1899) 4: 255–332 gave a comprehensive picture of his general outlook, with references to his earlier papers. For the paper with observed and calculated v_m values for 66 compounds, see "Über das Molekularvolumen," *Berichte* 28 (1895): 2722–2728. He somewhat modified and extended his views in some later papers; see note 29.

29. The review "Über den Raum der Atome" (note 28) is the most convenient source for Traube's interpretation of the covolume. His later paper "Ueber Atom- und Molekularraüme," *Annalen der Physik* 5 (1901): 548–564, developed his ideas somewhat further. In this he proposed other ways of estimating the volume *b*, independently of the summation of atomic volumes, making use of an equation proposed by van't Hoff for one calculation, and deducing volumes from molar refractivity in another approach. This paper is also significant for his increasing emphasis on the variability of atomic volumes.

30. The quotation from "Über den Raum der Atome" is on p. 276; that from his *Annalen* paper of 1901 is on p. 550. See notes 28 and 29.

31. The first paper by Richards bore the title "The possible significance of changing atomic volume." Omitting the word "possible," the later papers used the same general heading. The subtitles were: "II. The probable source of the heat of chemical combination, and a new atomic hypothesis. III. The relation of changing heat capacity to change of free energy, heat of reaction, change of volume, and chemical affinity. IV. The effects of chemical and cohesive internal pressure." They were published in English in the *Proceedings of the American Academy of Arts and Sciences* 37 (1901): 1–17; 37 (1902): 397–411; 38 (1902): 291–317; 39 (1904): 581–604; and in German translation in *Ztschr. Physik. Chem.* 40: (1902) 169–184, 597–610; 42: 129–154; 49 (1904): 15–40. When quoting from Richards I use the original version in English.

32. Richards plotted the data for the change of enthalpy (ΔH) and of free energy (ΔF) as a function of temperature, and extrapolated them so as to indicate that they would tend to converge at 0°K. As G. N. Lewis remarked later, "Except for the fact that these cells involved solutions, the curves presented by Richards very nearly imply the generalizations which were later to be embodied in the third law of thermodynamics." See G. N. Lewis and M. Randall *Thermodynamics* (McGraw Hill, New York 1923) 437. This passage is not given in the revised version of Lewis and Randall by K. S. Pitzer and L. Brewer, 1961.

   Nernst formulated his heat theorem in 1905, but made no mention of the work of Richards; an omission that Richards strongly resented. How far Richards may have perceived the larger implications of his findings is doubtful. Nernst evidently considered that Richards had not perceived them; see the article on Nernst by Erwin Hiebert in the *Dictionary of Scientific Biography* 15, 432–453.

33. The first quotation from this paper is on p. 581, the first text-page of the English version. The footnote regarding Traube's work is on p. 583. The final sentence of this note is omitted in the German translation. The reference to W. Müller-Erzbach is to his paper: "Die Volumverhältnisse bei der Bildung und Umsetzung von Sauerstoffsalzen im Vergleich mit den dabei entwickelten Wärmemengen," *Berichte* 14 (1881): 217–222, with a related paper in the *Annalen der Physik und Chemie,* Neue Folge 13: 528, which I have not seen. Müller-Erzbach stated clearly a correlation between volume contraction and heat of reaction, and this had been called to Richards's attention, as noted in his second paper.

34. Traube sets forth these general views most explicitly in "Die Eigenschaften der Stoffe als Funktionen der Atom- und Molekularräume und Gedanken über die Systematik der Elemente," *Zeitschr. für Anorganische Chemie* 40 (1904): 372–384; but many of them are already well developed in "Über den Raum der Atome" (note 28).

35. Traube had put forward this general conception in a paper of 1894: "Die Grundlagen eines neuen Systems der Elemente," *Berichte* 27: 3179–3181. He repeated and elaborated his views in the references cited in notes 28, 29, and 34. In the "Lebenserinnerungen," while recognizing the great illumination provided by the work of Rutherford and Bohr, he

still maintained the general value of his views on atomic volumes.

36. P. Drude and W. Nernst, "Über Electrostriktion durch freie Ionen," *Ztschr. Physikal. Chem.* 15 (1894): 79–85.

37. I. Traube, "Über die Ursache des osmotischen Drucks und der Ionisation." *Ztschr. Anorg. Chem.* 8 (1895): 323–337. In "Raum der Atome", 330 (note 28) and again in the "Lebenserinnerungen," 41, he reaffirmed this view and rejected the electrostriction hypothesis. We may note that, after 1920, J. N. Brønsted and others rewrote the equation, for ionization of such molecules as acetic acid, as HAc + $H_2O \rightleftharpoons Ac^- + H_3O^+$. On this basis there is no change in the number of particles when such an acid ionizes, but simply a proton transfer from the acid to water. However one cannot expect that Traube in 1895 could possibly have thought along such lines.

38. Elliot Quincy Adams, "Relations between the constants of dibasic acids and of amphoteric electrolytes," *J. Amer. Chem. Soc.* 38 (1916): 1503–1510. Niels Bjerrum, "Die Konstitution der Ampholyte, besonders der Aminosäuren, und ihre Dissoziationskonstanten," *Ztschr. Physik. Chem.* 104 (1923): 147–173. An English version is in N. Bjerrum, *Selected Papers.* (Munksgaard, Copenhagen 1949), pp. 175–197. Bjerrum did not refer to Adams, and was obviously unaware of his work at that time.

39. See E. J. Cohn, T. L. McMeekin, J. T. Edsall and M. H. Blanchard, "Studies in the physical chemistry of amino acids, peptides and related substances. I. The apparent molal volume and the electrostriction of the solvent," *J. Amer. Chem. Soc.* 56 (1934): 784–794. There are several other related papers from Cohn and his associates in the same journal (1935–36) and the results are collected in Cohn and Edsall, "Proteins, Amino Acids and Peptides" (see note 19) 155–165. I might add that all of us in those days took electrostriction for granted. We found Traube's atomic volumes and covolume values very useful for calculation, but had failed to notice his disagreement with Drude and Nernst. Indeed I became aware of it only on reading the "Lebenserinnerungen," and then reexamining Traube's early papers.

For the background of this work at Harvard Medical School, which also involved George Scatchard and John G. Kirkwood at M.I.T., and Jeffries Wyman in the Harvard Biological Laboratories, see J. T. Edsall, "Edwin Joseph Cohn (1892–1953)," *Biog. Mem. Nat. Acad. Sci.* 35 (1961): 47–84; and J. T. Edsall and W. H. Stockmayer, "George Scatchard (1892–1973)," *Biog. Mem. Nat. Acad. Sci.* 52 (1980): 335–377.

40. This passage, including the quotation from Raoult, is from "Lebenserinnerungen," 6–7. Traube does not give a reference for the quotation, and I have not found it in a cursory search of Raoult's writings; but it does reflect his general point of view.

41. See "50 Jahre Arbeit" (note 3), p. 1.

42. This account is based on "Lebenserinnerungen," 4–10. Traube gives the complete text of the letters

from Lothar Meyer and Walden, which I have briefly summarized here. Walden was a major figure in German and Russian chemistry, distinguished in physical chemistry and stereochemistry, discoverer of the stereochemical inversion that bears his name, and a learned historian of chemistry. In the Nazi era he followed a very different course from that of the exiled Traube. Walden remained in Germany and made himself acceptable to the régime, publishing articles concerning German chemistry and its "national way." These certainly did not constitute blatant Nazi propaganda, but they were probably well calculated to be acceptable to the authorities. When war came, he was indeed to know calamity: an air raid on Rostock in April 1942 totally destroyed his house, with its precious library of some ten thousand volumes. He and his wife escaped with their lives, but for some five years they were wanderers, until they found a haven in Tübingen in 1947. There he died peacefully ten years later at 93. See Walter Hückel, "Paul Walden: 26 July 1863–22 Januar 1957," *Chemische Berichte* 91, (1958): XIX–LXVI. Walden's own posthumously published autobiography *Wege und Herbergen: Mein Leben,* (Franz Steiner, Wiesbaden 1974, 130 pp) contains much of personal and scientific interest, but only one paragraph (pp 109–110) touches on his life during the Nazi era. Here he paints a dark picture, of the tragic effects on the young of the reversal of values, with destructive insane ideas and gross lies being propagated. He says that his modest charitable contributions went primarily to Jewish friends. One of his closest friends and collaborators, from his earlier days in Riga, Professor M. Centnerszwer, was brutally murdered in the Warsaw Ghetto; to him this was "a stab in the heart." Nevertheless, he emphasized, he was irrevocably attached to Germany; "to have left Germany would have been my own inner downfall." It was Germany that had offered him a haven and a professorship in Rostock, after his many years in imperial Russia, when he and his family fled from the Soviet Union after the revolution. One must remember that Walden's account was written years after the downfall of the Nazis; one cannot expect it to be an accurate picture of his attitude and emotions at the time. Nevertheless, in my own judgment, it probably contains much truth. Walden was a sufficiently important figure to deserve further study, and I add this note to encourage others to investigate him and his work further.

43. J. H. van't Hoff, "Die Rolle des osmotischen Druckes in der Analogie zwischen Lösungen und Gasen," *Zeitschr. Physik. Chem.* 1 (1887): 481–508. S. Arrhenius, "Über die Dissociation der in Wasser gelöste Stoffe," ibid, 631–648. Arrhenius's views had been largely developed in a memoir submitted to the Swedish Academy of Sciences in 1883, and van't Hoff had presented a memoir to the Academy in 1885, but it was their papers in 1887 that attracted worldwide recognition among chemists.

44. This quotation from van't Hoff is taken from the

English translation of his paper in the Alembic Club reprints, No. 19 (Edinburgh 1929) p 7. This volume also contains a translation of the Arrhenius paper.

45. L. Meyer, "Über das Wesen des osmotischen Drucks," *Zeitschr. Physik. Chem.* 5 (1890): 23–27; J. H. van't Hoff, "Antwort an Herrn Lothar Meyer," ibid, 174–176. Dolby, "Debates over the Theory of Solution" (note 2), 377–380, gives an excellent discussion of the confusion over osmotic pressure that persisted for some twenty years after van't Hoff's paper appeared. See also 351–352 and 366–369 in Dolby's paper. Willard Gibbs gave a thermodynamic proof of van't Hoff's law: "Semi-permeable films and osmotic pressure," *Nature* 55 (1897): 461 (reprinted in the *Collected Works of J. Willard Gibbs*, Vol. I, 413–417, Longmans Green, New York and London 1928) but the later paper of G. N. Lewis probably did more to clarify the subject for most chemists. G. N. Lewis, "The osmotic pressure of concentrated solutions, and the laws of the perfect solution," *J. Amer. Chem. Soc.* 30 (1908): 668–683. See also Lewis and Randall, *Thermodynamics*, 1923, pp. 234–236, for a straightforward thermodynamic derivation of van't Hoff's law.

46. I. Traube, "Über die Dissociationshypothese von Arrhenius," *Berichte*, 23 (1890): 3519–3530. Ostwald's caustic *Referat* on this paper is in *Z. Physik. Chem.* 7 (1891): 91. Arrhenius replied to Traube in *Berichte*, 24 (1891): 224–231. Traube published four further related papers in the same volume, with another reply by Arrhenius on pp. 2255–2264. This paper contains the critique of Traube's freezing point measurements. This controversy can also be followed in the correspondence of Ostwald with Arrhenius and van't Hoff; see Hans-Günther Körber (editor). *Aus dem wissenschaftlichen Briefwechsel Wilhelm Ostwalds*, 2. Teil. (Berlin: Akademie-Verlag 1969). The references to Traube can be readily found in the index. Ostwald takes a consistently contemptuous attitude toward Traube.

For Traube's 1892 paper see Traube, "Die Hypothesen der elektrolytischen Dissociation und der Ionisation," *Berichte* 25: 2989–2993. In the "Lebenserinnerungen," p. 42, he states particularly clearly the idea that a single ion is associated with a single water molecule, although they can readily change places with other water molecules. On the same page is the citation of Poynting's views (see below). The reference Traube gives to Poynting is in *Ann. der Physik* 62 (1897): 495. Poynting also appears in Dolby's discussion (note 2) p. 348.

47. The letters from Poynting and Fitzgerald are quoted in "Lebenserinnerungen," 12–13. Poynting's letter is dated 21 December 1897; no date is given for Fitzgerald's. Dolby (note 2) discusses the role of these two physicists in the Anglo-German debate over the ionization theory; for Fitzgerald see pp. 332–337, and 346–348. His Helmholtz Memorial Lecture to the Chemical Society was given in 1896; see *J. Chem. Soc.* 69: (1896) 885–912. Concerning Poynting see p. 348 of Dolby.

The Arrhenius theory evidently troubled many physicists. As a student in the course in physical chemistry given at Harvard by Theodore W. Richards (1922–23) I heard him tell of meeting Lord Kelvin around 1890. Kelvin warned him against the Arrhenius theory, saying in effect: "Young man, it cannot be correct. It is fundamental in electrostatics that a collection of freely mobile charges cannot remain in equilibrium. They are bound to reassociate." Richards however became an early convert to the Arrhenius theory in spite of this warning.

Traube portrays himself as the lone critic of the Arrhenius ionization theory among the German physical chemists. This is probably an exaggeration. Erwin Hiebert has noted that, about 1891, "The scientists associated with Wiedemann in Berlin were beginning to band together into an outspokenly hostile anti-ionist front." Hiebert names Rüdorff in Berlin, and Ladenburg in Breslau, along with Traube, among these critics. See E. N. Hiebert: "Developments in Physical Chemistry at the Turn of the Century," in *Science, Technology and Society in the Time of Alfred Nobel*, C. G. Bernhard, E. Crawford and P. Sörbom, editors (Oxford, Pergamon 1982), pp. 97–115. The quotation is from p. 104. Hiebert refers to the Ostwald correspondence with Arrhenius and van't Hoff (note 46) as the basis for these comments.

Nevertheless Traube's sense of isolation on this issue was probably real. By the middle 1890s Ostwald dominated the German world of physical chemistry; new professorial appointments in the field were likely to be Ostwald's pupils or disciples. Traube, who was seven years younger than Ostwald, was probably thinking of his own contemporaries who were competitors for good appointments in physical chemistry, not of the few senior critics of Arrhenius who were already in established positions. Compared to his contemporaries he was at a formidable disadvantage in seeking a good professorial appointment at a leading institution.

48. I. Traube, *Grundriss der Physikalischen Chemie*, vii + 360 pp. (Stuttgart, Verlag von Ferdinand Enke 1904). The section on the Arrhenius theory is on 188–198. Ostwald reviewed the book unfavorably in *Ztschr. Physik. Chem.* 50 (1905): 252–253. On the other hand Traube quotes a note from Sir William Ramsay, saying that Traube's textbook was the only scientific book he was taking with him on a trip to Switzerland; and the distinguished chemist Clemens Winkler also wrote him a warm note of appreciation about the book. However no second edition ever appeared; Ostwald's review was very likely decisive in killing the possibility of further editions.

49. The passage quoted above, and the following discussion, is based on I. Traube, "The Attraction Pressure," *Journal of Physical Chemistry* 14 (1910): 452–470. This appears to be a translation of his paper: "Die Theorie des Haftdrucks (Oberflächendrucks) und ihre Bedeutung für die Physiologie." Pflüger's *Archiv für die gesamte Physiologie* 132

(1910): 511–538; also see ibid, 140 (1911): 109–134. Another long paper in English by Traube is: "The cohesion pressure: A theory of solution," *Ion* 1 (1909): 312–355. I know nothing of this journal, but a copy of the paper is in one of the bound volumes of Traube's papers in the E. F. Smith Library in Philadelphia, with others of his papers in foreign languages.

50. I. Traube, "Zur Geschichte der modernen Lösungstheorien und der Theorie des Haftdrucks," *Kolloid-Beihefte* 37 (1933): 119–153; with editorial note by Wo. O., pp. 152–153.

51. J. H. Wolfenden, "The anomaly of strong electrolytes," *Ambix* 19 (1972): 175–196.

52. On p. 13 of the "Lebenserinnerungen," Traube, after quoting most of Wolfgang Ostwald's comment (which I have set down above in translation) speaks with considerable bitterness over the fact that his name was not remembered by the younger workers on the physical chemistry of electrolytes, and that most of the journals where he might have written on this subject were closed to him.

53. See Traube, "50 Jahre Arbeit," 5. The relevant passage, in the original German, reads (Traube speaks of himself in the third person):

"Im Jahre 1891 habilitierte sich Traube an der Technischen Hochschule zu Berlin für physikalische Chemie. Leider! Denn, wenn er auch im Jahre 1898 eine Dozentur erhielt und im Jahre 1900 den Titel Professor, so hat er doch trotz mancher Leistungen, um welche ihn manche Ordinarien beneiden könnten, nichts als Zurücksetzung in Anbetracht gewisser in der Abteilung massgebenden Persönlichkeiten auch mancherlei Demütigungen erfahren müssen. Er hat sich schliesslich dazu verstehen müssen, der Not gehorchend, die allgemeine physikalische Chemie mit Kolloidlehre zu vertauschen und bezieht jetzt im Alter von 70 Jahren das fürstliche Gehalt von 4500 Mark ohne Pensionsberechtigung!

"Zahlreiche Arbeiten sind aus Traubes Laboratorium in dieser Zeit hervorgegangen, obwohl Traube lange Jahrzehnte weder Assistent, weder genügende Mittel noch geeignete Schüler hatte."

54. Overton made other important discoveries. As early as 1896 he recognized the phenomenon of active transport, in which a substance moves across a cell boundary against a concentration gradient, i.e. in the opposite direction to that of simple diffusion. He observed that sodium ions in the surrounding fluid were essential for the irritability of muscles and nerves, and perceived the possibility of relations between sodium and potassium ions, in these tissues, that were established, half a century later, by A. L. Hodgkin, A. Huxley and B. Katz. Overton never published his intended full account of his work on permeability; ill health in later life, and his work as a university teacher and administrator, prevented it. He never bothered to reply to the rather numerous critics of his views. Very few scientists have been so influential with so few publications: only some 25 papers, and a short monograph *Studien über die Narkose, zugleich ein Beitrag zur allgemeinen Pharmakologie,* (G. Fischer, Jena 1901). For biographical information see P. R. Collander, "Ernest Overton (1865–1933): a Pioneer to Remember," *Leopoldina* 8–9 (1962–63) [3]: 242–254; and W. Url, "Charles Ernest Overton—75 Jahre Lipoid Theorie," *Verhandlungen der zoologisch-botanischen Gesellschaft in Wien* 115 (1976): 24–33. For a brief account of Overton by Collander, see *Dictionary of Scientific Biography* 10: 256–257.

Concerning H. H. Meyer, see A. Jarisch, "Hans Horst Meyer" in *Ergebnisse der Physiologie, Biologischen Chemie und Experimentelle Pharmakologie* 43 (1940): 1–8. Meyer's first paper on the subject is: "Zur Theorie der Alcoholnarkose. I. Welche Eigenschaften der Anästhetika bedingt ihre narkotische Wirkung?" *Archiv f. experimentelle Pathologie und Pharmakologie* 42 (1899): 109–118.

55. Traube, "Theorie der Osmose und Narkose." *Arch. für die ges. Physiol.* 105 (1904): 541–558. "Die Oberflächendruck und seine Bedeutung im Organismus," ibid 105: 559–572. Also: "Theorie der Narkose" ibid 218 (1928): 749–766, and various papers in *Biochem. Zeitschrift,* from Vol. 54 (1913) to 120 (1921): 111–124 (the latter paper with P. Klein). See also the references cited in note 48. This list is a good sample of Traube's views, but makes no attempt at completeness. He gives a comprehensive view of his biological researches in "Lebenserinnerungen," 70–91.

56. "Lebenserinnerungen," 70. Jarisch, in his memoir on Meyer (note 54) points out that Meyer came to consider that the conflict between the "chemical" and the "physico-chemical" schools was becoming resolved by the increasingly detailed knowledge of the structure and dynamics of molecules, which was bridging the gap in outlook between the organic and the physical chemists.

57. See references cited in note 55, and especially I. Traube and P. Klein, "Experimentelle Beiträge zur Theorie der Narkose," *Biochem. Zeitschr.* 120 (1921): 111–124.

58. For Traube's quotation from Höber about "a flood of papers" with Traube's comment, see "Über Narkose," *Biochem. Ztschr.* 54 (1913): 316–322. The quotation and comment are on p. 322. My comments on Höber's book are based on the fifth edition of *Physikalische Chemie der Zelle und der Gewebe,* Volume I (1922) and Volume II (1924), (Leipzig: Wilhelm Engelmann.) Chapter 7, in Vol. I, is on permeability; Chapter 8, in Vol. II, deals with narcosis. For Bayliss *General Physiology* I have consulted the third edition (London, Longmans Green 1920).

59. O. Warburg, "Über die Verbrennung der Oxalsäure an Blutkohle und die Hemmung dieser Reaktion durch indifferente Narkotika," *Archiv f. die ges. Physiol.* 155 (1914): 547–558. The passage quoted is on p. 548. This article is reprinted in O. Warburg, *Über die katalytischen Wirkungen der lebendigen Substanz,* (Berlin, Julius Springer 1928) 35–46. The remarks of Warburg concerning Traube in 1928, cited

above, are from p. 2 of the introductory article in this book, which bears the same title as the book. Warburg cited in particular the paper by Traube, "Theorie der Narkose," *Archiv für die ges. Physiol.* 153 (1913): 276–308, which also gives references to Traube's earlier work.

60. Traube, "Theorie der Narkose," 1928. See note 55. I. Traube and F. Dannenberg, "Über das Permeabilitätsproblem," *Biochem. Zeitschr.* 198 (1928): 209–224.

61. For Traube's views on the problem of cancer, see "Lebenserinnerungen," 89–91. Here he cites an article, "Carcinom, Pflanzenwachstum, Oberflächenspannung und Permeabilität," *Zeitschrift für Krebsforschung* 28 (1929): 356, which as yet I have not seen.

62. For these and other activities, see "Lebenserinnerungen," 91–99.

63. There is a file of the *Internationale Zeitschrift*, bound in two volumes, in the Traube collection at the Edgar Fahs Smith Library, University of Pennsylvania. The publisher was Wilhelm Engelmann (Leipzig and Berlin). Traube believed that the *Zeitschrift* might have survived and prospered after the war if Engelmann had not become discouraged.

64. Ramsay's letter to Traube (in German) is on p. 58 of "Lebenserinnerungen."

Extinction[1]

George Gaylord Simpson

Introduction and Early Retrospect

"Si se opone la naturaleza lucharemos contra ella y haremos que nos obedezca."[2] (Quotation from Simón Bolívar now on the wall of the house where he was born in Caracas. His subject was not extinction, but his remark and attitude are appropriate for the current investigations of extinction as it occurs in nature.)

The subject of extinction has long been discussed and now even more than ever. There are still some questions as to just what extinction is, how it can or should be defined. Still more searching are attempts to enumerate and to place the geological times of greater or lesser extinction. Recently even more varied and at times more vehement have been hypotheses or supposed proofs of causes of extinction, whether in general, or in particular groups of organisms, or at specified episodic times.

Nowadays there is probably no one aware of the subject who does not agree that extinction, by some definition, has occurred in some species or other taxon, at some time or another, however much the disagreement on each particular of this general statement. It may then be surprising that for many years in the history of philosophy of science involving biology there was wide agreement that extinction by any definition, of any group of organisms, or at any time did not occur. A summary of this peculiar historical fact may serve as background for explicit attention to more recent ideas about extinction.

Although other Greek philosophers had skirted similar topics, Plato is generally credited with holding among his multitude of philosophical terms and thoughts one which he discussed but did not explicitly name. Lovejoy (1936) proposed that this Platonic conception be called the "principle of plenitude." In effect, it seemed to mean that everything, whether perfect or imperfect, that can exist does exist. It is evident that this excludes the nonexistence of anything, and therefore the extinction (or ceasing to exist) of anything. Although he was a student of Plato, Aristotle did not accept the principle of plenitude in quite the Platonic form. He did appreciatingly note the great diversity of organisms, but he considered that all of nature falls into a set of transitions that are graded from the most imperfect to the most perfect. This became the basis for what was later called in Latin the "scala naturae," and eventually in French the "échelle des êtres" and in English the "great chain of being." (Again see Lovejoy, 1936; also Osborn, 1913; and on this point especially Mayr, 1982.)

Aristotle further provided the basis for two other lines of thought that continued to be held sometimes almost dogmatically even into the early nineteenth century. One was spontaneous generation: the continual origin of relatively imperfect organisms from nonorganic matter. Another was the inheritance of acquired characters.

What eventually came to be known as fossils of extinct organisms were known to some of the ancient Greeks. Nevertheless through all of the generations from Aristotle, who died in 322 B.C., to Cuvier, who was born in A.D. 1769, the evidence for the real-

ity of extinction was usually either explained away or ignored. The continuity of Platonic and Aristotelian concepts through the eighteenth century is especially well illustrated by Buffon, who lived from 1707 to 1788. Assisted by others, notably Daubenton, he started a tremendous work on natural history, the "Histoire Naturelle," which eventually filled 44 volumes (Buffon et al., 1749–1804). Early in this work Buffon wrote, "It is possible to descend by almost insensible degrees from the most perfect creature to the most formless matter." This implied a complete continuity among simultaneous existing forms of matter, from animate perfection (human beings, of course) to the inorganic. At that time Buffon believed that species were artifacts and did not exist in nature. In a later volume of the same work he changed his mind and wrote that species are realities and are "the sole beings of nature." Some historians have seen Buffon's vacillation as tending toward a concept of evolution, but he continued to view species as segments in a single échelle des êtres and as permanent as nature itself.

It is nevertheless true that there are gaps between known species and that this fact became evident to Buffon and to other naturalists who continued to have faith in the continuity among existing species. This was explained away by postulating that species that would fill in the gaps exist but had not yet been discovered. In fact Buffon and his colleague Daubenton were acquainted with fossils of genera and species now known to be extinct, mostly mammoths and mastodons. They concluded that some of the bones were simply variations among elephants, therefore not of extinct species. Daubenton (1764) did see that some of the mastodon teeth were quite unlike those of elephants, but he referred to them as variant hippopotamuses. Thomas Jefferson, the most versatile of American presidents, was acquainted with remains of extinct mastodons

as early as 1781 and with some parts of what was later recognized as an extinct ground sloth in 1797. Yet in 1825 (a year before his death) he let stand his earlier conviction, as follows: "Such is the economy of nature, that no instance can be produced of her having permitted any one race of animals to become extinct; of her having formed any link in her great work so weak as to be broken."

Jefferson's view was orthodox in his day, and had been so ever since Aristotle or earlier. The earliest and even then only tentative suggestion that I have found in contradiction of this ancient belief was written by a then well-known British anatomist, William Hunter in 1768. He demonstrated that what he called the "American *incognitum*" and what we call *Mammut americanus* or "the American mastodon" was a species distinct from the living African elephant, but he thought (incorrectly) that it was probably the same as the Siberian mammoth. He went on to say that, "If this animal was carnivorous, which I believe cannot be doubted, though we may as philosophers regret it, as men we cannot but thank Heaven that its whole generation is probably extinct." That mastodons were carnivorous was in fact doubted even then, and of course has now long been known to be untrue, but this error did lead Hunter into a first hint that species might become extinct. (See also Simpson, 1942.)

LAMARCK AND CUVIER

Although Lamarck (1744–1829) was 25 years older than Cuvier (1769–1832) he lived 22 years longer, and their lives overlapped widely. Both became eminent zoologists, both spent most of their careers in Paris, and both were early connected with what came to be known as the Jardin des Plantes. Works by both are relevant to the history of studies of evolution and of extinction, but, as will here be briefly considered, in very different, in fact diametrically opposite, ways.

Lamarck's most important works were his *Histoire naturelle des animaux sans vertèbres* published in seven volumes from 1815 to 1822 and the *Philosophie zoologique* published in two volumes in 1809, which coincidentally was the year of Darwin's birth. It is that work (1809) that concerns us here.

In the introduction ("avertissement") Lamarck wrote in his now somewhat obsolescent and even then not very polished French:

Should I not think that nature had sequentially produced the different bodies endowed with life by proceeding from the simplest toward the most complex; since going up the animal ladder from the most imperfect animals to the most perfect the organization is built up and even gradually complicated in its composition in an extremely remarkable way?

Farther along, in Chapter V of the First Part of the *Zoological Philosophy*, Lamarck listed his fourteen "classes," the same word in French as in English and as in classifications still in use. They were then placed "in an order contrary to that in nature," that is, with the most advanced (Mammals) first and the least advanced (Infusoria, or approximately what we would now call Monera and Protoctista) last. Farther along Lamarck reversed the sequence, arguing or rather stating that the order in nature went in opposite direction, from the simplest to the most complex. It was then an example or an important part of the *scala naturae*, which Lamarck wrote of as the "animal ladder" ("échelle animale") or "chain" (chaîne animale). He also called it a "series" (série).

Still farther along, in Chapter VIII of the First Part, Lamarck wrote:

Indeed, if it is true that all the living organisms are products of nature, one cannot but believe that she [nature/GGS] has only been able to produce them in succession and not all at once in a time without deviation. There is reason to think that it is only with the simplest that she began, having produced only last of all the most complex

organisms either of the animal kingdom or of the vegetable kingdom.

This and the *Philosophie zoologique* as a whole is a definite statement that all existing organisms arose by evolution during a vast extent of time. Although he did not himself use the word "evolution," he was the first to state unequivocally that evolution is the explanation of the origin of all living species.

Beyond that he maintained that animals, at least, reacted to environmental influences by the needs and uses of the parts of each individual and that the results were passed on to their progeny. This involved another concept, that of the inheritance of acquired characters, which was not new but was as old as Greece. Note that it was the reactions of individuals to environments and not any direct effects of the latter that were supposed to produce hereditary changes. He also adopted the ancient Greek belief in the spontaneous generation of animals at the beginning of the "échelle."

At the end of the second volume and part of the *Philosophie zoologique* Lamarck wrote additions to the crucial chapters VII and VIII of the first volume and part. He here moved beyond or at least modified his belief in a single ladder or chain of being. In a text and diagram ("tableau") of animal evolution he here comments and shows that in his latest view he considered that the "ladder" (échelle) of animals began by two distinct branches and that some divergent parts of them seem to end at certain points. In text and diagram he indicated and discussed what would now be called an evolutionary phylogeny. It is true that further knowledge has made nonsense of much of this. Lamarck had birds arising from turtles and mammals from crocodiles, except for the monotremes which are shown as a dead end evolved from birds. That would seem to imply, at least, that in the long, slow climbing up the ladder there existed, for example, species interme-

diate between turtles and birds. As no such animals were then or have ever been known, one could conclude that in one sense of the word those intermediates are now extinct. However, Lamarck did not consider this as extinction. For him the series, ladder, or chain that led to birds still lives, *as* birds.

Lamarck thus envisioned evolution without extinction. When his major work was published, his unfriendly colleague Cuvier was already beginning to expound the opposite concept, that of extinction without evolution.

As early as 1799, ten years before Lamarck's *Philosophie zoologique*, Cuvier was already publishing on fossils of species considered extinct, in this case "elephants" including the extinct mastodons. From 1804 to 1810 he published many other papers on fossils of extinct vertebrates. With some revision, these were collected and published in 1812 as the four volumes of the first edition of *Recherches sur les ossemens fossiles* (1812). Although this was some years after fossils of extinct animals had been described by Cuvier himself and several others, it is generally considered as the principal basis for paleontology as a distinct science. The first volume of this work began with a long (116-page) *Discours préliminaire* which could be considered as Cuvier's "zoological philosophy" in addition to and as an attack on that by Lamarck. With extensive revision it was repeated in later editions of the *Recherches* (1821–1824), and was finally published as a separate volume in French in 1825. English and German translations of the *Discours préliminaire* had then already been published. Reference here is to the 1825 French edition.

By 1825 it had been well established by Cuvier himself and by other early stratigraphers and paleontologists that there is a sequence of strata containing fossils and that the fossils differ with respect both to geographical occurrence and to relative geological ages. There was thus an already clear

although as yet very incompletely known sequence of faunal and floral changes in the course of geological time. Cuvier held that most of the fosils known to him, and especially those in the early strata, were extinct, and extinct without issue. He firmly denied that there was an *échelle des êtres.* He had early observed that the known living organisms did not demonstrate an Aristotelian or a Lamarckian sequence. Even more firmly he denied that any organisms of today have evolved from different ancestral forms.

Cuvier maintained that the history of the earth and of its animals and plants was punctuated by a series of revolutions, in each of which many extinctions occurred. The last of these revolutions could be equated with the great flood described in the seventh chapter of the book of Genesis. As a confirmed Christian and Protestant in a predominantly Catholic country this interpretation placed Cuvier in an apparently impossible position. If there was a whole sequence of mass extinctions followed by quite different genera and species, must there not have been also an equal sequence of divine creations? As is more fully discussed in the excellent biography of Cuvier by Coleman (1964), this was an apparent impasse for Protestant Christianity, and Cuvier cleverly dodged it. He said that while he held that various genera and species had become extinct, he did not find that it was necessary for a new creation to produce the species still existing. He said only that the surviving species had not been living in the same places where one finds them at present, and that they must have come from somewhere else. As an example, he went on to say that if Australia ("Nouvelle-Hollande" to Cuvier) were to be flooded by the sea all the marsupials and monotremes confined to that continent would become extinct and would be known only as fossils. If then a land connection with Asia were formed by that same revolution, the continent of Australia would be occupied by elephants, rhinoceroses, buf-

falos, horses, camels, tigers, and all the other Asiatic animals which would come to occupy a land where they had not previously been known. (In fact such a local revolution did not occur in Australia, but one somewhat like Cuvier's fantasy did occur in South America.)

DARWIN

Thus far we have followed in barest outline concepts of the living world from the ancient Greeks, with important steps taken especially by Lamarck and Cuvier. The next and overall the most important step of all was taken by Darwin. A part of that sequence has been followed at greater length than is possible here in a well-written, recent book by Browne (1983), especially covering the period from Athanasius Kircher (1602–1680) through that of Charles Darwin (1809–1882). Browne is primarily concerned with ideas about the origins of species and their subsequent biogeography, but she does also consider extinction and provides background for changing concepts regarding it. Valuable as this is, it does seem that she has not quite clearly followed Cuvier's *Discours* in connection with extinction, perhaps because she is primarily interested in botany but Cuvier was not (neither was Lamarck). The *Discours* does not support Browne's view that Cuvier was a "directionalist" who believed that there was "advancement" through time rather than simply change of localities after a single creation of all animals (and plants) at once.

As has now been briefly expounded, Lamarck gave us evolution of a sort *without* extinction, and Cuvier gave us extinction of a sort *without* evolution. It was Darwin who among many other things gave us evolution *with* extinction.

From the start of his career as a scientist Darwin was well aware of the fact that a great many animals had become extinct. During the voyage of the *Beagle* Darwin was studying Lyellian geology. In the second volume of Lyell's great *Principles of Geology* (1832) the first edition, which Darwin had with him, Lyell wrote of the successive extinction of terrestrial and aquatic species as "part of the economy of our system." A page later he added that "amidst the vicissitudes of the earth's surface [as previously discussed in Lyell's first volume/GGS] species cannot be immortal, but must perish one after another, like the individuals which compose them."

It is thus not surprising that in his first published account of his voyage on the *Beagle* (1839), Darwin, still a creationist as was Lyell at that time, wrote:

We see that whole series of animals, which have been created with peculiar kinds of organization, are confined to certain areas. . . . On such grounds it does not seem a necessary conclusion that the extinction of species, more than the creation, should exclusively depend on nature (altered by physical changes) of their country. All that at present can be said with certainty, is that, as with the individual, so with the species, the hour of life has run its course, and is spent.

Somewhat later, in 1846, although he was then already writing, but not publishing, in evolutionary terms, Darwin published in Lyellian terms that the extinction of "great mammifers" (large fossil mammals) in both North and South America was due to the "ice-age," the Pleistocene epoch in modern terms. The implication was that the change in climate brought about that mass extinction, a point still under discussion and here to be more particularly noted below.

Darwin's later evolutionary publications from the first edition of "On the Origin of Species . . ." in 1859 onward, frequently referred to extinction, its results, and in generally somewhat indefinite terms its causes. In the first edition (1859) there are more than a dozen mentions of extinction. The subject was discussed briefly in Chapter IV, on natural selection, and at length in Chapter X on

geological succession. In the earlier chapter of the two Darwin noted: "Rarity, as geology tells us, is the precursor to extinction. We can, also, see that any form represented by few individuals will, during fluctuations in the seasons or in the number of its enemies, run a good chance of utter extinction." "Geology," in this connection paleontology, does not invariably show us a clear reduction in sizes of populations leading to extinction, and it is nearly a truism that reduction of population size to zero is extinction by a usual definition. However Darwin here does suggest material causes of such reduction: seasonal fluctuation (which in the sixth edition of the *Origin* Darwin changed to "great fluctuations in the nature of the seasons"), or changes in the number of "enemies," which could mean either competitors or predators.

In Chapter X of the first edition of *The Origin of Species*, which became Chapter XI in the now more widely accessible sixth edition, Darwin carried these ideas further, devoting more than five pages to a section "On Extinction." Here Darwin used the term "group" in the taxonomic sense of genera, families, or other collective taxa of species of common origin. He made several points still worthy of, and receiving, attention today. He wrote that some groups have persisted since the then earliest known dawn of life but that others disappeared during the Paleozoic, there being "no fixed law" as to the length of time for groups. He added that: "There is reason to believe that the complete extinction of the species of a group is generally a slower process than their production." On these points, although wording it differently, Darwin clearly anteceded the supposedly new theory called "punctuated equilibrium" by its recent proponents.

Although maintaining that the origin of a group, by multiplication of species, is usually more rapid than its extinction, Darwin did also note that in some cases the extinction

of whole groups "has been wonderfully sudden." As examples he notes the apparently sudden extinction of trilobites at the close of the Paleozoic and of ammonites at the close of the "secondary" (now called "Mesozoic"). Darwin went on to suggest that the apparent abruptness of such mass extinctions may be due to intervals of time for which there were (when Darwin wrote) no known continuity of strata and that hence there are gaps in the [handwritten manuscript continues here] fossil record.

When the extinctions seem to have been more gradual, Darwin advanced two not necessarily conflicting hypotheses. One, considered as evidence for natural selection, was that "the improved and modified descendants of a species will generally cause the extermination of the parent species." Along this line of thought competition was postulated as a cause for extinction of some groups or species and survival of others, later in origin. A second of Darwin's hypotheses was that groups and species do fluctuate in the numbers of individuals and the geographic areas occupied. When either of these fluctuating values happens to reach zero, obviously extinction has occurred. This defines a question and not an answer, however hypothetical that may be. Darwin's words as to that were more profound than clarifying: "If we ask ourselves why this or that species is rare, we answer that something is unfavorable in its conditions of life; but what that something is, we can hardly ever tell."

As will hereafter be discussed, since Darwin we have amassed more data and multiplied hypotheses, but we still "can hardly ever tell" what the causes of extinction are in general or in most particular instances.

SOME DEFINITIONS AND SOME PROCEDURES

It may seem strange that it is necessary to define extinction beyond a definition such as the biological definition in a widely used

college dictionary: "The act or process of becoming extinct or dying out." In fact there are at least three different kinds of extinction, so that clarity demands definition not only of extinction in general but also of the three different, although sometimes intergrading, kinds.

The most general technical definition of extinction can be given as the cessation of a taxon at any level to continue *as such*. *As such* is stressed because it is essential for definition of one of the now usually recognized modes of extinction. This mode or type of extinction is variously called "pseudoextinction," "taxonomic extinction," or "phyletic extinction." That occurs when in the course of evolution a taxon changes enough to be recognized taxonomically different but the continuation of a former line of direct descent. An example at the specific level is the taxonomic sequence of *Homo erectus*, which according to the current consensus evolved into *Homo sapiens*. By this view, *Homo erectus* is pseudoextinct.

An example at higher taxonomic levels is given by the evidence that the class Mammalia, and hence all its orders, clearly evolved from members of the order Therapsida of the class Reptilia. The great majority of the suborders, families, genera, and species of Therapsida were terminally extinct at or before the end of the Triassic period. Nevertheless at least two and quite possibly three or four of the lineages within the Therapsida certainly evolved into mammals and thus were only pseudoextinct. That does not mean that the Therapsida are not extinct *as such*, nor does it warrant and still less does it require reclassifying the mammals as Therapsida. That would be as absurd as classifying the birds (Aves) as dinosaurs, which has actually been done, although not by a paleontologist.

The term extinction is most often used in the sense of terminal extinction, meaning that at whatever level as a taxon it was a group that has absolutely no living descendants. [Manuscript ends here.]

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    "But if indeed the extinction of the gigantic carnivorous marsupials of the Deseadan [early Oligocene/GGS] should be connected with the extinction of their large prey, obviously the deeper causes should be sought in the climatic-environmental changes, modifiers of the bases (roots) of the trophic chain."
Doello-Jurado (1939). In conclusion—
    ". . . On comparing these two kinds of biological facts, individual death and *phyletic death*, the cause of which escapes us, one does not know how to say whether we

have enlarged the scope of our knowledge or that of our ignorance."

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NOTES BY LÉO F. LAPORTE

1. When he died at age 82 on 6 October 1984, George G. Simpson had this essay on extinction in preparation. It comprised 13 pages of typescript, two pages of corrected, handwritten manuscript, a bibliography, and several pages of notes. Anne Roe, his wife, and I thought it would be of scientific and historic interest to make available this last, unfinished work by a leading contributor to modern evolutionary theory on a subject that has always intrigued students of life history. This and subsequent footnotes as well as bracketed remarks are by Léo

F. Laporte (Earth Sciences, Univ. of California, Santa Cruz, CA 95064) to whom reprint requests should be addressed.

2. "If nature is opposed, we will fight her and make her obey us."

3. The following is a list of references that Simpson apparently intended to use for his essay. At the end of this section I provide a briefly annotated bibliography of these references, arranged alphabetically by author.

The references listed by Simpson indicate that he intended a major discussion of how to interpret extinction, both pseudoextinction and phyletic extinction as well as mass extinctions. Apparently, he was to consider the role of habitat destruction and the interdependence of species in their demise; he also seems to have wanted to link extinction rates with speciation rates. It is clear, too, from his list that he was not to give any special priority to extraterrestrial causes of extinction. Of course, these comments are highly speculative and we have no real way of knowing the final content and emphasis of Simpson's essay. Simpson's last, extended discussion of extinction can be found in Chapter 5, "Extinction, Origination, and Replacement," in his book, *Fossils and the History of Life*, 1983, Scientific American Books, W. H. Freeman and Co., New York, p. 122–150.

A New Look at Medieval Cosmology, 1200–1687*

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Attitude toward Scholastic Defenders of Aristotelian Cosmology

To speak of medieval cosmology as ranging from 1200 to 1687, virtually the end of the seventeenth century, may appear to some yet another instance of medieval temporal imperialism. Why should the sixteenth century and 87 years of the seventeenth century be embraced by the Middle Ages? To this question, there is only one plausible response: despite serious challenges, medieval cosmology, based solidly on the cosmic conceptions of Aristotle, remained the dominant worldview until 1687. When, in 1632, Galileo published his monumental assault on Aristotelian cosmology, the *Dialogue on the Two Chief World Systems*,[1] the majority of astronomers and natural philosophers were probably defenders of traditional Aristotelian geocentric cosmology, a cosmology that had been shaped in the thirteenth and fourteenth centuries. There are as yet no good reasons for believing that the situation had altered significantly by 1687, some fifty-five years after Galileo's *Dialogue* and 144 years after publication of Copernicus's *On the Revolutions of the Heavenly Spheres (De Revolutionibus)*.[2] But in that fateful year, the year chosen as the terminal date for scholastic Aristotelian cosmology,[3]

Isaac Newton published his *Mathematical Principles of Natural Philosophy*.[4] Copernicus's heliocentric system, with its Keplerian modifications, was at last provided a physical basis that made continued support for Aristotle's geocentric cosmology untenable. After 1687, medieval cosmology became irrelevant because it no longer represented even a minimally plausible alternative to the new Newtonian cosmology. Unlamented it simply faded away.

If medieval cosmology was dominant from 1200 to 1687, and therefore an intellectual force to be reckoned with during the 144 years that were required for the total triumph of the Copernican system, why is this not properly reflected in the great mass of research on seventeenth-century science and natural philosophy that has appeared in this century? Why is our knowledge of it derived primarily, but indirectly, from its enemies, rather than directly from studies of the literature? With a few possible exceptions, we look in vain for evidence of genuine interest in the last century of scholastic cosmology.[5] What accounts for this virtual absence of interest in the arguments and defenses of one of the major sides in the debates that raged in the seventeenth century? Is it because, as one historian has recently declared, "in science as in war history is written by the victors" and "those who first embraced a new science are styled precursors of the latest orthodoxy. Those who stubbornly clung to the

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old are featured as historical curiosities. One group is absorbed, the other is absurd."[6] Although this perceptive description was formulated for Christian anti-Darwinians in their struggle against Darwinism, it is even more relevant and applicable to the scholastic Aristotelians who defended medieval cosmology against Copernicanism. Those who upheld the fixity of species have been studied for their own sake in the totality of research on the history of nineteenth-century biology. Even phlogiston theory has been studied for its role in the history of eighteenth-century chemistry. But serious considerations of Aristotelian scholastic cosmology are absent from researches on seventeenth-century science and cosmology. The names, works, and ideas of late sixteenth- and seventeenth-century scholastic authors have all but disappeared from sight. Perhaps the victors in the cosmological struggle did indeed banish the vanquished to historical oblivion.

In fact, they banished them even before the victory. Beginning with the late sixteenth century, those who supported the developing new science and cosmology rarely cited scholastic authors except, on occasion, to attack and ridicule them.[7] Instead of Aristotelian scholastics, they cited Greek and Roman authors, along with recent and contemporary mechanical philosophers, Hermeticists, Platonists, Neoplatonists, Stoics, and Atomists. By a seeming conspiracy of silence, scholastic authors were largely absent from the body of literature that would be of greatest interest to modern scholars. Even Galileo, who clashed directly with scholastic natural philosophers—especially the Jesuits Christopher Scheiner and Horatio Grassi—rarely mentioned their names in published works, largely because, for various reasons, his foes chose to attack by the use of pseudonyms and surrogates.[8]

But as if ignominious silence were not enough, fate, in the guise of Galileo Galilei, dealt an even harsher blow. For Galileo's most enduring assault on scholastic Aristotelian cosmology derived from a fictional character whom he named Simplicio, after the sixth-century Greek Aristotelian commentator, Simplicius. Simplicio, who first appears in the *Dialogue on the Two Chief World Systems*, Galileo's major attack on Aristotelian cosmology, became almost immediately the paradigm of the dull-witted, unimaginative, unyielding scholastic defender of the indefensible. Although the circumstances of publication made a direct, unrestrained, and scornful critique of Simplicio's Aristotelian cosmology unwise, Galileo left little doubt of his sympathies and attitude. Although many Aristotelians would accept the telescope as a valid scientific instrument, Simplicio is made to declare that "following in the footsteps of other Peripatetic philosophers of my group, I have considered as fallacies and deceptions of the lenses those things which other people have admired as stupendous achievements."[9] The slavish dependence on Aristotle is emphasized when, in denying that the earth is an orbiting planet, Simplicio appeals to Aristotle, who, according to Simplicio, raised serious, unresolved objections to such an opinion. "And since he [Aristotle] raised the difficulty without solving it, it must," insists Simplicio, "necessarily be very difficult of solution, if not entirely impossible."[10] In this manner Galileo achieved, perhaps unwittingly, more than he might have thought possible. By his literary and artistic genius, he fashioned a stereotype and caricature that has been applied to all scholastic Aristotelian scholars from their emergence around 1200 to their effective demise near the end of the seventeenth century. More than anyone, Galileo created the concept of a monolithic, homogeneous, unimaginative, inflexible Aristotelianism, which, when finally challenged by Copernicanism in the sixteenth and seventeenth centuries, reacted as a whole in the manner of Simplicio: it blindly rejected all that was new by opposing to it one or an-

other of the many dogmas of Aristotle. On this approach, there are no significant differences between the scholastic contemporaries whom Galileo flayed in the seventeenth century and their medieval predecessors in the thirteenth and fourteenth centuries. This is undoubtedly the popular and, to a large degree, even the learned conception of medieval cosmology that prevails to this day.

It is small wonder that modern scholars have ignored the final century of scholastic Aristotelian cosmology. They found little mention of scholastic authors in the works that formed the corpus of the new and developing science of the seventeenth century and what they did learn from Galileo was enough to convince them that any further examination of scholastic literature would only yield more Simplicio-like pronouncements. After three centuries of neglect, however, it is time to take another look at medieval cosmology in the late sixteenth and seventeenth centuries. To do that with any hope of genuine comprehension, it is essential to look at the whole of medieval cosmology. Only then will it become apparent that that whole is not monolithic and homogeneous but rather divides naturally into two distinct and considerably different parts, each of which is itself unhomogeneous.

THE TWO PARTS OF MEDIEVAL ARISTOTELIAN COSMOLOGY

The first part embraces the period from approximately 1200, when the works of Aristotle were translated into Latin and began to have an impact, until approximately 1500, when a new wave of translations was underway. During the first period, Aristotelian cosmology had no rivals and went unchallenged. Disagreements about interpretations of major and minor points of Aristotle's cosmology during this period were always of an internal nature.[11] There is no hint of abandoning that system in favor of anything else.[12]

But all this was destined to change. Already in the 1460s, rival cosmologies and new ideas began to appear. The works of Plato and those attributed to Hermes Trismegistus were translated from Greek to Latin, as a great new wave of translating activity got underway in Italy.[13] By the mid-sixteenth century cosmological concepts and reports embedded in previously unknown works by Sextus Empiricus, Plutarch, Simplicius, Philoponus, Themistius, Alexander of Aphrodisias, Lucretius and Cicero were available. The worldviews of Plato, the Stoics and Atomists were now potential rivals to Aristotle. In works falsely and rightly attributed to Plutarch were descriptions of the earth's axial and orbital motions.[14] The probability is strong that even if Copernicus had never written the *De revolutionibus*, a significant debate about the earth's possible axial and orbital motions would have occurred.

But in 1543 Copernicus did publish his *De revolutionibus* and, by his conviction that the earth really rotated daily on its axis and also orbited the sun annually, posed the most dangerous challenge to the Aristotelian geocentric worldview. Not long after, Tycho Brahe demonstrated that the new star of 1572 and the comet of 1577 were actually celestial phenomena and not alterations in the upper atmosphere just below the moon, as Aristotelians believed.[15] The implications were profound: the new star struck a seemingly vital blow at the Aristotelian concept of an absolutely unchangeable and incorruptible celestial region while the comet, thought by Tycho to be moving in a circular orbit around the sun,[16] seemed to destroy the traditional belief in hard, celestial spheres to which the planets were attached and by which they were moved. Such hard spheres would either have prevented the comet from traversing its observed path, or would have been shattered by its impact. In the early seventeenth century, 1611 to be exact, Galileo, Christopher Scheiner, and Johann Fa-

bricius observed variable spots on the sun, which some would interpret as another blow against celestial incorruptibility.[17]

Confronted with these momentous new challenges, scholastic Aristotelians of the late sixteenth and seventeenth centuries reacted in a wide variety of ways, ranging from those who drew upon the store of traditional explanations and who wrote as if nothing new had occurred since the thirteenth century[18] to those who adopted the geoheliocentric system of Tycho Brahe. Incredible as it may seem, in at least one instance scholastic opinion even extended to the acceptance of the heliocentric system itself. In a treatise titled *Peripateticall Institutions* and published in 1656, Thomas White, a theologian, who considered himself a faithful Aristotelian, though admitting that his conclusions sometimes dissented from the master, concluded that wind-driven seas caused the earth to rotate daily and, because of an unequal impact on the earth's surface, those same seas also pushed the earth laterally and caused it to move with an orbital motion around the sun.[19] Thomas White is admittedly an anomalous case but should serve as a warning that seventeenth-century scholastics are not easy to categorize. Nor indeed are medieval scholastics, who, without any pressure to defend the Aristotelian system, often disagreed on points of cosmological doctrine. Because of the direct challenge of the Copernican system to the Aristotelian, however, seventeenth-century scholastics were under greater pressure and their responses, not surprisingly, were far more varied than anything found in the Middle Ages, as we shall now demonstrate.

DEPARTURES FROM MEDIEVAL COSMOLOGY

1. Celestial Incorruptibility[20]

Following the introduction into Western Europe of Aristotle's scientific treatises during the twelfth and thirteenth centuries, medieval natural philosophers assumed with Aristotle that the world was divided into two radically different regions, the terrestrial, which embraced everything below the concave surface of the lunar sphere, and the celestial, which included the sphere of the moon and everything beyond to the farthermost reaches of the finite cosmos. An important ingredient of Aristotle's two-region cosmology was the conviction that the celestial region was incomparably superior to the terrestrial. That superiority was most dramatically manifested by the attribution of absolute incorruptibility to the celestial region, which was said to be composed of an incorruptible ether.[21] By contrast, corruptibility seemed an obvious property of terrestrial bodies, which were subject to incessant, perceptible changes. Aristotle had seemingly clinched his case for celestial incorruptibility when he declared that no changes in the celestial region had ever been observed or recorded.[22] If the heavens were corruptible, some obvious sign of it should have been detectable over a long period of time. But what about shooting stars, comets, and other similar phenomena which seem to appear in the heavens? Are these not transient celestial phenomena that indicate changes in the heavens? Not according to Aristotle, who simply denied their celestial location and placed them instead in the upper atmosphere just below the moon. He explained them as products of the various motions of hot and dry terrestrial vapors in the region just above air.[23] By the elimination of such potential counterinstances, Aristotle made the historical record serve the cause of incorruptibility. It is small wonder that celestial incorruptibility won near-unanimous acceptance between the thirteenth and late sixteenth centuries. During that same period, it was also assumed that the incorruptible ether was shaped into hard spheres to which the planets and stars were attached and by which they were carried around the heavens in circular orbits.

These beliefs, which were conceived as fundamental during the Middle Ages, were, as already seen, seriously challenged in the

late sixteenth and early seventeenth centuries by Tycho Brahe, Galileo, and others. Some of those who accepted these discoveries and the new interpretations were prepared to accept dramatic changes in the nature of the heavens. Observations of the new star, comet and sunspots taken together convinced many that the celestial region could no longer be assumed incorruptible; telescopic observation of sunspots offered startling evidence that even the familiar and seemingly unalterable planets were subject to change; and the apparent lack of resistance to the comet of 1577 as it moved around the sun implied an absence of hard, transparent celestial spheres.

How did scholastic authors react to these seemingly grave dangers to Aristotelian cosmology? Before replying to that question, it is well to keep in mind that, with a few exceptions, most seventeenth-century scholastics were not only aware of the new Copernican cosmology, but also knew about the discoveries and claims of Tycho Brahe and Galileo. Nevertheless, many doggedly defended the traditional opinions. Following Aristotle, they insisted that the new star of 1572, the comet of 1577, and the spots on the sun's surface were in reality phenomena of the upper atmosphere, much as Aristotle had described them in his *Meteorology*.

But changes in approach would soon become apparent. A number of scholastic authors found Aristotle's responses inadequate to the challenges they confronted. Tycho Brahe's reputation as an observational astronomer was not to be set aside lightly. And so it was that some scholastics accepted the new stars and even comets as celestial phenomena generated in some manner within the celestial region itself. But this did not mean that they were prepared to abandon their belief in celestial incorruptibility. Their problem now was to explain the "new" celestial phenomena without abandoning incorruptibility.

Leaving aside the possibility that new stars and comets were supernatural creations,

which few believed, two major approaches were devised to reconcile celestial incorruptibility with the celestial location of new stars and comets. One approach constructed new stars and comets from bodies already preexisting in the heavens, while the other assumed their formation from accidental—not substantial—changes that actually occurred in the heavens.

The first approach made implicit use of Galileo's discovery of the satellites of Jupiter. Here were celestial bodies that had always been in the heavens but remained unseen until revealed by Galileo's telescope. Was Galileo's discovery only the tip of the iceberg? Was it not reasonable to suppose that many other permanent, but ordinarily invisible, fixtures of the sky were awaiting discovery?[24] And, to take it a step further, perhaps some celestial bodies were so faint that one could never hope to see them even with a telescope. The stage for the introduction of celestial phantoms was now set. Thus, as Stillman Drake has observed, "Conservative astronomers who for philosophical reasons had previously rejected Galileo's discovery of new moving stars in the heavens, now for philosophical reasons commenced to populate the sky with moving stars at a rate which made Galileo blush."[25]

To save celestial incorruptibility, invisible heavenly bodies were now postulated as needed. Indeed this practice had begun even before Galileo's discoveries, as we learn from Christopher Clavius (1537–1612), the famous Jesuit astronomer, who reports that a few explained the new star as a magnification of a regular, but ordinarily invisible, star in the constellation Cassiopeia.[26] Its emergence as an *apparent* new star was caused by terrestrial exhalations that were interposed between us and the star. Following Galileo's celestial discoveries, the practice intensified, as is evident in the discussions of Bartholomew Amicus (1562–1649), a Jesuit theologian who described at least four ways in which new stars might be formed from already existing celestial matter, only two of

which will be mentioned here.[27] One way was to assume that a number of small, ordinarily invisible, stars would somehow come into alignment and form a sufficiently large mass capable of reflecting light and thus becoming visible. Another way, which Amicus favored, was to assume the existence of epicycles each of which carried a denser than normal piece of celestial ether. When, for example, three such epicycles came into alignment, the sun, which shines on the whole heaven, would illuminate that ethereal cluster, the reflected light of which then produces the appearance of a new star. As the epicycles continue with their uniform motions, the new star will gradually fade away. On this approach, celestial changes are not real but only apparent. Combinations and dissociations of already existing entities are said to produce the new but transient phenomena.

Not long after Tycho Brahe had declared that the New Star of 1572 was located in the celestial region, Christopher Clavius also declared unequivocally for this interpretation.[28] Thus early on, we find at least one scholastic who found the evidence for a celestial location convincing, or, conversely, found the evidence for a sublunar location quite unconvincing. The New Star had to be higher than the region of the air because it would have revealed different aspects at such a close distance, whereas none had thus far been observed. Thus it had to be in the celestial region. But it could not be in any of the regular planetary orbs because no astronomer had yet detected any other motion for the new star. Therefore, argues Clavius, it must be in the firmament, or sphere of the fixed stars. Moreover it could not be in the elementary region because there would then be no plausible explanation as to why it always maintained the same distance and relative position with respect to the other fixed stars.

As to the origin of the star, Clavius declared that it was either created by God as a major portent, or if it was a natural celestial event, then one would have to concede that comets could also be created in the heavens, just as they could be created in the air. But if the latter alternative is true, then perhaps "the heaven is not a certain fifth element, but a mutable body, although less corruptible than inferior [terrestrial] bodies." [29] Prior to Plato and Aristotle, many philosophers believed this and indeed after those two luminaries, some of the most eminent Church Fathers—Ambrose, Basil, and Gregory of Nyssa—taught the corruptibility of the heavens.

But just as we expect Clavius to take a daring stance and opt for the corruptibility of the celestial region, he declares that he does not wish to interpose his opinion in this matter (*meam enim sententiam in tanta re non interpono*).[30] He is content to have demonstrated that the new star is in the starry firmament. As for all the other difficult questions associated with the new star—what it portended, why it vanished after two years, and so on—Clavius insisted that only God knew the answers. Thus in his most famous and widely used book, Clavius opted for the real existence of the new star but chose to avoid any commitment to the perplexing questions about the corruptibility or incorruptibility of the celestial region. But there were other scholastics who also came to believe in the celestial location of the new star, but, unlike Clavius, emphatically maintained the traditional belief in celestial incorruptibility. They were convinced that the new celestial phenomena represented real, and not merely apparent, changes. One such was Raphael Aversa (1589–1671), who, though he assumed a sublunar origin and location for comets, allowed that new stars represented real celestial change.[31] How could real celestial change be reconciled with incorruptibility? By assuming, as Aversa did, that new stars are formed by accidental rather than substantial changes. To make his case, Aversa assumed that parts of the heaven

were transparent and parts opaque rather than rare and dense.[32] Transparency and opacity are qualitative properties and the changes associated with them are accidental, whereas rare and dense are quantitative properties and the changes associated with them are substantive. To avoid substantial changes in the heavens, Aversa abandoned the properties rare and dense, and insisted that the ethereal matter of the heavens could only be transparent and opaque. A qualitative change occurs when a diaphanous part of the heaven becomes sufficiently opaque to reflect light and become visible as a star; as the star's opacity diminishes, however, the ability of the ethereal substance to reflect light diminishes and the new star gradually disappears. Although Aversa confessed ignorance as to the cause or causes that could transform a part of the celestial ether from transparent to opaque and back again to transparent, he thought that he had defended celestial incorruptibility by replacing the essentially quantitative terms rare and dense by the qualitative terms transparent and opaque.[33]

By the third quarter of the seventeenth century, at least three Jesuit authors—Giovanni Baptista Riccioli (1598–1671), Melchior Cornaeus (1598–1665) and George de Rhodes (1597–1661) abandoned the traditional scholastic belief in the incorruptibility of the heavens. Riccioli, the most famous scholastic astronomer of his day, believed that "from its very internal nature, the heaven has the capacity for generation and corruption."[34] Riccioli based his belief in celestial corruptibility on three sources,

namely the authority of Sacred Scripture, the testimony of the Fathers, and the arguments derived from experience concerning spots and torches near the solar disk that were discovered by the telescope and from certain comets that have come into being and passed away above the moon. These changes are more naturally explained by generation and corruption than by other more violent means or by nonviolent miracles.[35]

Of these three sources, however, Riccioli was influenced most by the Church Fathers who convinced him that the heavens were composed of two elements that were identical with their terrestrial counterparts, namely water and fire, with the former composing the solid sphere of the fixed stars and the latter comprising the planetary heavens, which Riccioli conceived as a fiery fluid.[36] Because water and fire formed a vital aspect of terrestrial change, Riccioli, like the Church Fathers he claimed to follow, believed they were also involved in celestial generations and corruptions. With Riccioli, Cornaeus, de Rhodes, and others, the claims of Tycho Brahe and Galileo were accepted without qualification.

2. Fluid Medium and Tychonic System

With regard to the issue of celestial incorruptibility, we see that scholastics in the seventeenth century adopted a variety of positions, ranging from acceptance of the traditional medieval position to its complete repudiation. A similar range of reactions could be cited for other cosmological issues in the seventeenth century. Because the celestial path of the comet of 1577 would have destroyed, or been affected by, solid planetary spheres, Tycho Brahe rejected the existence of solid spheres and assumed instead a fluid medium through which comets and planets were self-moved.[37] In this significant break with Aristotle and the Middle Ages, a number of scholastics followed Tycho, as did, for example, Roderigo de Arriaga, Franciscus Bonae Spei, and Franciscus de Oviedo,[38] while others—Riccioli, for example—accepted the fluidity of the heavens but retained the solidity of the sphere of the fixed stars.[39] Some scholastics, including Bartholomew Mastrius, Bonaventura Bellutus, Giovanni Baptista Riccioli, and Melchior Cornaeus, even adopted Tycho Brahe's cosmological system in whole or in part.[40] That is, they located the stationary earth in the

center of a spherical universe and assumed that at least two, and perhaps all, of the other planets moved around the sun as their center of motion with the sun, in turn, orbiting the earth.

3. The Terraqueous Sphere

Another instance of a significant departure from medieval cosmology concerned the physical description of the earth itself. The change involved a shift from the medieval view, in which one sphere each was assigned to earth and water, to a single sphere concept in the seventeenth century that included both earth and water and which came to be called the "terraqueous sphere."[41] Because it was obvious that parts of the earth rose above the sphere of water, it was assumed during the Middle Ages that the sphere of water surrounded the sphere of earth in a manner that left only a quarter of the earth's sphere elevated above the waters. The habitable portion of the earth's sphere was said to lie wholly in the northern hemisphere with the southern hemisphere completely submerged. The Portuguese explorations of the southern hemisphere, especially a voyage along the coast of Brazil in 1501, revealed a wide distribution of land in the southern hemisphere that was previously thought to be submerged. In 1515, Joachim Vadianus of Switzerland proclaimed that not only did earth and water together form a single globe, but their relationship was such that over the entire surface of that globe earth is partly submerged and partly elevated. Here was the first description of what would be called the "terraqueous globe" in the seventeenth century.[42] But even before it was named, Copernicus adopted it in his De revolutionibus.[43] The concept entered scholastic cosmology in the late sixteenth century when Christopher Clavius embraced it in his famous and widely read Commentary on the Sphere of Sacrobosco.[44] During the seventeenth century, most scholastic natural philosophers assumed that earth and water formed a single, unified sphere and so abandoned the two separate spheres of the Middle Ages. On this point, at least, scholastic natural philosophers were au courant.

THE RELATIONS BETWEEN MEDIEVAL AND EARLY MODERN SCHOLASTIC COSMOLOGY

From the examples just described, it seems reasonable to assume that early modern scholastic Aristotelian cosmology did indeed depart considerably from its medieval counterpart. May we infer from this that early modern scholastics were more flexible and innovative than their medieval predecessors? Such an inference would be unwarranted. Indeed a careful comparison between the two might well reveal that medieval cosmologists were more imaginative and venturesome. Why, then, did early modern scholastics depart more radically from Aristotelian cosmology than did scholastics in the Middle Ages? In my judgment, the answer lies, as already indicated, in the new external challenges to the Aristotelian system that began to take effect in the sixteenth century. Significant alterations in Aristotelian cosmology made in the Middle Ages continued to be discussed into the seventeenth century, as, for example, the possible existence of an infinite extracosmic void space[45]; the existence of eccentric and epicyclic spheres[46]; and the identification of celestial and terrestrial matter.[47] These medieval innovations were well known to scholastics in the seventeenth century. But seventeenth-century scholastics were confronted with a situation that had no precedent in the Middle Ages. They had not only to contend with a heliocentric cosmology that was virtually the antithesis of their own, but even more important they had to cope with astronomical discoveries and interpretations that challenged the very existence of the traditional solid spheres, the incorruptible heavens, and the two-region cosmos. With such formi-

dable threats to the system, it is small wonder that significant changes occurred.

It was the external threat that caused scholastic Aristotelian cosmology to undergo major alterations in the seventeenth century. The disagreements that arose in the Middle Ages about particular aspects of the prevailing Aristotelian cosmology did not produce serious challenges to the system as a whole. But things were quite different in the late sixteenth and seventeenth centuries. Galileo is perhaps the best illustration of the dramatic changes. With considerable justice, Galileo may be viewed as an Aristotelian who abandoned the system. Whether or not Galileo's Aristotelian treatises—the so-called *Juvenilia*—actually reflect his true opinions, it is reasonable to assume that in his youth his opinions about natural philosophy were largely Aristotelian because he had been so educated. But already in the *De motu*, which forms part of the *Juvenilia*, Galileo attacked Aristotle's explanation of natural and violent motion as well as his concept of absolute light and heavy.[48] Similar criticisms, however, had already been made in the Middle Ages[49] and, although Galileo's critiques were presented more systematically, they were not radically different from what could be found earlier. At some point, however, Galileo learned about the Copernican system and when, in 1597, in a letter to Kepler,[50] he declared himself a Copernican, we may conclude that Galileo no longer believed in the fundamental structure of the Aristotelian cosmos. But Galileo could shift cosmological allegiance because he had an option. Potential Galileos in the fourteenth century had no such options. Whatever their dissatisfactions with Aristotelian cosmology, they had no serious alternatives and continued to operate in the traditional framework, accepting as systemic the various anomalies that had emerged.

The first significant and dramatic alternative to Aristotle's cosmology was, of course, the Copernican. The emergence of that incredibly important option does not appear to have been directly or intimately associated with the scholastic cosmological tradition. It surely was not the outcome of internal critiques within the Aristotelian system itself.[51] If anything, it is more likely the product of the new Renaissance currents of sixteenth-century Europe. With its appearance in 1543, however, Copernican cosmology represented a powerful alternative to the Aristotelian. It was a challenge that could not be ignored.

Aristotelians now realized that they had to defend more seriously than ever before their claims for the earth's centrality and immobility.[52] Because there were as yet no convincing means to demonstrate the truth of the heliocentric system, that defense would have been feasible were it not for the more threatening inferences that Tycho Brahe drew from the new star of 1572 and the comet of 1577 and the equally devastating consequences of Galileo's telescopic discoveries, especially those that followed from the discovery of sunspots.

In the cosmological controversies of the sixteenth and seventeenth centuries, some abandoned Aristotelian cosmology and became Copernicans. Many of these subsequently also adopted the celestial location of new stars, comets, and sunspots. But many remained Aristotelians. Their reaction to the new challenges was, as we have argued, varied. Some not only abandoned celestial incorruptibility and solid spheres, but even accepted Tycho Brahe's geoheliocentric system in which all the planets orbited around the sun and the latter, in turn, moved annually around the earth, which was immobile in the center of the cosmos.[53] At least one scholastic, and perhaps more, assumed that the earth was more perfect than the sun, which implies an abandonment of the fundamental Aristotelian idea that the celestial region is more perfect than the terrestrial.[54] Indeed, we even saw that Thomas White assumed the physical reality of the heliocentric

system. Such actions—especially the last mentioned—by avowed Aristotelians raises a significant question: is a core of Aristotelian cosmological belief distinguishable without which the appellation "Aristotelian" becomes meaningless? or was the Aristotelian system so capacious that it could even absorb major ideas that were antithetical to its own authentic and well-established concepts?

What has been shown here thus far indicates that Aristotelian cosmology, and especially Aristotelian natural philosophy as a whole, was unusually capacious throughout the period of its existence.[55] It absorbed ideas that at first glance appear subversive of the system if their consequences had been pursued.[56] Such consequences, however, were either undetected or ignored and in those rare instances where cognizance was taken of them they were made compatible with the system. Thus Aristotelians seemed capable of living with serious anomalies that should have focused attention on inconsistencies within the system as a whole. Rather than draw damaging inferences from anomalous concepts and ideas, they successfully isolated and compartmentalized them.[57]

Were there concepts, however, which, if adopted by Aristotelians, would, by their very natures, have destroyed the system or emptied the expression "Aristotelian cosmology" of significant content? I should want to argue that at least one belongs to this category, namely the heliocentric system itself. To accept the earth as a planet no different from any other of the traditional planets and to have it orbit around the sun assumed at rest at or near the center of the cosmos would have made Aristotelian cosmology indistinguishable from the Copernican system. Virtually all that made the Aristotelian system distinctive would vanish, most notably the centrality and immobility of the earth and the sharp distinction between the celestial and terrestrial regions and with it presumably the capacity of the former to cause change in the latter.

How then shall we explain Thomas White, who, as we saw earlier, assumed the truth of the Copenican system and yet considered himself an Aristotelian? In reply, it is essential to understand that these are not incompatible concepts. Insofar as White accepted the heliocentric system, we must conclude that he had effectively abandoned Aristotelian cosmology. But he could nonetheless continue to consider himself an Aristotelian if he retained other significant aspects of Aristotelian natural philosophy. He might have continued to believe in Aristotle's principles of biology and perhaps also Aristotle's explanations of change, and so on. Indeed there were Aristotelians in the eighteenth and nineteenth centuries (for example, in logic, biology, and metaphysics) who were undoubtedly heliocentrists and would hardly have considered themselves Aristotelians in cosmology. During the Middle Ages most, if not all, were Aristotelian natural philosophers in the full sense, that is, they subscribed to Aristotle's natural philosophy as a whole although they might disagree with particular explanations. But as particular aspects of Aristotelian natural philosophy were repudiated and overthrown or simply abandoned, the term Aristotelian has to be more carefully specified. In cosmology, some, as we saw, rejected celestial incorruptibility and solid spheres and at least one person also assumed the axial rotation of the earth,[58] but all quite reasonably considered themselves Aristotelians because all retained belief in a geocentric universe. To my knowledge, Thomas White is the only exception, the only one who considered himself an Aristotelian and embraced the heliocentric system. As the sole exception, and for the reasons already given, Thomas White should be considered an anomaly. Although Aristotelian cosmology was extraordinarily absorbtive of seemingly incongruous and even hostile concepts and ideas during the sixteenth and sevententh centuries, it was not so sponge-like that it could also absorb the heliocentric system.

CONCLUSION

By the seventeenth century, Aristotelian scholastic cosmology could hardly be characterized as "a many splendored thing." But neither was it a hopelessly static and congealed body of medieval doctrine, as it has so often been depicted. Based on the examples described here, it ought to be more accurately characterized as a body of varied opinion in which there was at least some genuine effort to incorporate aspects of the new cosmology into the old. Far from being monolithic, scholastic Aristotelians ranged from steadfast defenders of the status quo to those who actually came to oppose important elements of the Aristotelian system which they replaced with new ideas and observations derived from their opponents. And like some of their medieval predecessors, a few even came to view Aristotle with a more critical spirit, in a manner strikingly at variance with Galileo's depiction of the slavish and dogmatic Simplicio. Melchior Cornaeus, for example, in his defense of celestial corruptibility in 1657, sought to convince his readers that

If Aristotle were alive today and could see the alteration and conflagrations that we now perceive in the sun, he would, without doubt, change his opinion and join us. Surely the same could be said about the planets, of which the Philosopher knew no more than seven. But in our time, through the works of the telescope, which was lacking to him, we know for an absolute certainty that there are more.[59]

While paying tribute to Aristotle's scientific objectivity which would have prompted him to accept new and well-attested discoveries, Cornaeus also reveals a diminished confidence in Aristotle's cosmology. Indeed Franciscus Bonae Spei would declare that "in the books on *De caelo*, [Aristotle] erred many times."[60]

During the seventeenth century, many compromises were made. Bits and pieces of Aristotelian cosmology were replaced by bits and pieces of the new cosmology.[61] Strange cosmological mosaics were produced none of which could win widespread support. It was truly a period of transition. One system was passing away, another coming into being. To comprehend the momentous changes that occurred in the seventeenth century, it is essential to study the fate of the old cosmology as well as the new. Only then will we have a comprehensive picture of the cosmos as it was understood in the seventeenth century. Perhaps then we may learn, among other things, why Aristotelian cosmology coexisted with its Copernican rival for some 144 years before it succumbed.

NOTES

1. *Dialogo di Galileo Galilei Linceo . . . sopra i due massimi sistemi del mondo Tolemaico, e Copernicano* (Florence, 1632); reprinted in the National Edition: *Le opere di Galileo Galilei*, ed. Antonio Favaro, 20 vols. (Florence, 1890–1909), vol. 7.

2. Nicholas Copernicus, *De revolutionibus orbium coelestium* (Nuremberg, 1543).

3. As used here, the term "scholastic Aristotelian" applies largely to Catholic theologians who, for the most part, accepted Aristotle's philosophy of nature and cosmology and considered themselves Aristotelians. For further discussion and reasons for avoiding a definition of "Aristotelian" or "Aristotelianism," see Edward Grant, "In Defense of the Earth's Centrality and Immobility: Scholastic Reaction to Copernicanism in the Seventeenth Century," *Transactions of the American Philosophical Society*, 74, part 4 (1984), 3–4. Although I shall not offer a formal definition of "Aristotelian" or "Aristotelianism," I shall attempt below to consider criteria for being an Aristotelian in cosmology.

4. *Philosophiae Naturalis Principia Mathematica* (London, 1687).

5. Two possible exceptions are unpublished Ph.D. dissertations at Cambridge University by Christine Jones, "The Geoheliocentric Planetary System: Its Development and Influence in the Late Sixteenth and Seventeenth Centuries" (1964) and William H. Donahue, "The Dissolution of the Celestial Spheres 1595–1650" (1972). Although neither of these works was intended as a study of scholastic Aristotelian cosmological ideas in the seventeenth century, both contain much useful information about scholastic attitudes toward certain cosmological

concepts, namely the scholastic Aristotelian reaction to Tycho Brahe's geoheliocentric system and to the existence and nature of the celestial spheres. In both works, however, only the basic conclusions of scholastic arguments are presented; details are usually omitted.

6. James R. Moore, *The Post-Darwinian Controversies: A Study of the Protestant Struggle to Come to Terms with Darwin in Great Britain and America 1870–1900* (Cambridge: Cambridge University Press, 1979), 114. See also Grant, "In Defense of the Earth's Centrality and Immobility," 65.

7. There were of course exceptions, a notable one being Otto von Guericke, who cited numerous scholastic authors, including Leonard Lessius, Athanasius Kircher, and especially the Aristotelian commentaries of the Coimbra Jesuits (see his *Experimenta nova [ut vocantur] Magdeburgica de vacuo spatio* [Amsterdam, 1672; reprinted in facsimile Aalen: Otto Zeller, 1962], 51–52, 61–65).

8. See Stillman Drake, *Galileo at Work: His Scientific Biography* (Chicago: University of Chicago Press, 1978), 180, 489, n. 4; 264–273; also Drake, *Discoveries and Opinions of Galileo* (Garden City, N.Y.: Doubleday & Co., 1957), 81–82. In his attack on Christopher Scheiner, Galileo also used a surrogate, Mario Guiducci (see Drake, *Galileo at Work*, 267–268).

9. *Galileo: Dialogue Concerning the Two Chief World Systems*, translated with revised notes by Stillman Drake (Berkeley: University of California Press, 1962), 336. Although Simplicio immediately adds that "if I have been in error I shall be glad to be lifted out of it," there is no evidence that he was so lifted.

10. Ibid., 379.

11. There were numerous disagreements, as for example, whether eccentrics and epicycles were real or mere geometric conveniences; whether, if other worlds existed, more than one center could exist; whether the world was in a place; whether matter existed in the heavens, and so on. On all such issues, there were at least two opinions. But such "internal" disagreements did not produce opposition to the system as a whole and lead natural philosophers to devise a new system. Indeed in some of the disputes, each side claimed to be the faithful interpreter of Aristotle.

12. Although approximately two-thirds of Plato's *Timaeus* was available in Chalcidius's Latin translation during the Middle Ages, it posed no serious threat because most of Plato's other works were absent. Indeed Aristotle's cosmology had already confronted—and displaced—Plato's *Timaeus*, which was the basic cosmological text for scholars in the early Middle Ages prior to the introduction of Aristotle's physical works in the twelfth and early thirteenth centuries.

13. Although I am unaware of any single list of Renaissance translations from Greek to Latin, R. R. Bolgar has presented a list of "Greek Manuscripts in Italy During the Fifteenth Century" (R. R. Bolgar,

The Classical Heritage and Its Beneficiaries [Cambridge: Cambridge University Press, 1954], 455–505) and also organized a table of vernacular translations of Greek and Roman classical authors before 1600 (506–541). Not only did Renaissance humanists retranslate many works previously translated in the Middle Ages, but their more noteworthy contributions, according to Paul Kristeller (*The Classics and Renaissance Thought*, Martin Classical Lectures, vol. 15 [Published for Oberlin College by Harvard University Press, 1955], 16–17), lay "in those numerous cases where they translated works of Greek antiquity for the first time. The catalogue of these translations cannot yet be given in the present state of our knowledge, but it appears certain that the body of newly translated material includes practically all of Greek poetry, historiography, and oratory, much of Greek patristic theology and of non-Aristotelian philosophy, and even some additional writings on the sciences of mathematics and medicine. The authors, all or most of whose writings thus became known to Western readers, include Homer and Sophocles, Herodotus and Thucydides, Xenophon, Isocrates, Demosthenes, Plutarch and Lucian, Epicurus, Sextus and Plotinus, to mention only a few writers of obvious merit or influence. Again, dividing the line between works translated in the Middle Ages and first translated during the Renaissance often separates the individual writings of the same author, as is the case with Plato, Hippocrates, Galen, and Ptolemy, with many Aristotelian commentators and patristic theologians, and even with Aristotle."

14. See *De placitis philosophorum*, bk. 3, ch. 13, falsely ascribed to Plutarch but which was regularly included in the eleventh volume of Plutarch's *Moralia*; and see also Plutarch's *Concerning the Face Which Appears in the Orb of the Moon (De facie quae in orbe lunae apparet)*, p. 55 of Harold Cherniss's translation: Plutarch's *Moralia* with an English translation by Harold Cherniss and William C. Helmbold, vol. 12, 920A–999B (Loeb Classical Library; London: William Heinemann Ltd; Cambridge, Mass.: Harvard University Press, 1957).

15. Tycho's first publication on the New Star of 1572 was the *De nova et nullius aevi memoria prius visa stella . . .* (Copenhagen, 1573). His most important discussion of it appeared much later in *Astronomiae instauratae progymnasmata . . .* (Prague, 1602). The latter was the main source for subsequent summaries and descriptions in the seventeenth century. Tycho's account of the comet of 1577 did not appear until 1588 (shortly after the comet disappeared in 1578, Tycho wrote a German version that was not published until 1922), when he published the *De mundi aetherei recentioribus phaenomenis . . .* (Uraniborg). See C. Doris Hellman, "Brahe, Tycho," *Dictionary of Scientific Biography*, 2 (1970), 414; also 402–403 (on the New Star) and 406–409 (on the comet of 1577 and later comets). In the tenth chapter of the *De mundi aetherei*, Tycho summarized the opinions of contemporary astronomers on the comet

of 1577 and thus provided valuable historical data on that notable celestial event (see C. Doris Hellman, *The Comet of 1577: Its Place in the History of Astronomy* [New York: Columbia University Press, 1944], 120–121.

16. Hellman, "Brahe," *Dictionary of Scientific Biography*, 2 (1970), 408.

17. See Drake, *Discoveries and Opinions of Galileo*, 82–83. The Englishman Thomas Harriot seems also to have observed sunspots at about the same time.

18. One such was Juan Hidalgo, an Augustinian hermit, who, in a two volume treatise on natural philosophy based on the thought of Giles of Rome (Aegidius Romanus, ca. 1247–1316) and published in 1736–1737 (*Cursus philosophicus ad mentem B. Aegidii Col. Rom. . . authore R.P.M. Fr. Joanne Hidalgo Astigiensi . . .* [Cordova]), makes no mention of modern authors like Galileo, Copernicus, Tycho Brahe, Kepler, etc. Instead he follows Aquinas rather closely and cites quite a few of the major scholastic authors of the seventeenth century. Hidalgo seems caught in a thirteenth-century time warp.

19. On White, see my study "In Defense of the Earth's Centrality and Immobility," 8–9.

20. The present section on celestial incorruptibility is a highly abbreviated version of a paper that was delivered at an international workshop in Israel ("The Interrelations between Physics, Cosmology and Astronomy: Their Tension and Its Resolution 1300–1700," April 29–2 May 1984) and which will be published in the proceedings of the workshop.

21. See Aristotle, *De caelo*, bk. 1, ch. 3.

22. Ibid. 1.3.270b. 13–17.

23. Aristotle, *Meteorologica* 1.3.341a. 33–35 and 1.4.342a. 30–33.

24. In his thirteenth-century *Hexaemeron*, Robert Grosseteste already posed the questions that Galileo's telescopic discoveries would raise when he asked: "how is it known that there are not more planets, invisible to us but nevertheless useful and necessary for generation in the lower world? For the philosophers say that the Milky Way is made up of very small fixed stars, invisible to us. Therefore, how can it be known, except by divine revelation, whether there are not more stars of this sort invisible to us." Translated by Richard C. Dales, "The De-Animation of the Heavens in the Middle Ages," *Journal of the History of Ideas* 41 (1980), 541.

25. Drake, *Discoveries and Opinions of Galileo*, 83.

26. "Nonnulli enim, licet pauci, putaverunt, eam stellam novam non fuisse, sed unam ex antiquis illis tredecim quae semper in Cassiopeia ab astronomis sunt observatae; visam autem tunc esse maiorem solito propter exhalationem in suprema aeris regione inter ipsam et nostrum aspectum interiectam." *Christophori Clavii Bambergensis ex Societate Iesu in Sphaeram Iohannis de Sacro Bosco Commentarius* (4th ed.; Lyon, 1593), 208. Bartholomew Amicus mistakenly attributed this opinion to Clavius himself and added that the interposed exhalations made the star visible "just as a coin placed in water appears greater because of refraction." See Amicus,

In Aristotelis libros De caelo et mundo dilucida textus explicatio et disputationes in quibus illustrium scholarum Averrois, D. Thomae, Scoti, et Nominalium sententiae expenduntur earumque tuendarum probabiliores modi afferuntur (Naples, 1626), 246, col. 1. In fact, Clavius refutes this opinion (ibid., 210).

27. Bartholomew Amicus, *De caelo*, 244, col. 2 and 245, col. 2.

28. "Itaque ut breviter quod sentio, dicam, censeo stellam illam quaecunque illa fuerit in Firmamento ubi stellae fixae sunt extitisse." Clavius, *In Sphaeram Iohannis de Sacro Bosco Commentarius*, 210.

29. "Dicendum enim fortasse erit caelum non esse quintam quandam essentiam sed mutabile corpus, licet minus corruptibile sit quam corpora haec inferiora." Ibid., 211.

30. Ibid.

31. Raphael Aversa, *Philosophia metaphysicam physicamque complectens quaestionibus contexta* (2 vols.; Rome: Apud Iacobum Mascardum, 1625, 1627), 2, 91–100 (for arguments pro and con with an ultimate resolution in favor of the sublunar nature of comets), 85–86 (for the celestial nature of new stars). Aversa's opinion was rather similar to that of Galileo, who accepted the reality of celestial changes but did not declare in favor of the celestial nature of comets. In his *Discourse on Comets* of 1619 (although the work appeared under the name of Mario Guiducci, Galileo was unquestionably its author; see *The Controversy on the Comets of 1618: Galileo Galilei, Horatio Grassi, Mario Guiducci, Johann Kepler*, tr. Stillman Drake and C. D. O'Malley [Philadelphia: University of Pennsylvania Press, 1960], xvi–xvii) Galileo argued that astronomers had not yet demonstrated that comets were real bodies rather than reflections from vapors and therefore they were in no position to argue from parallax that comets were celestial (*The Controversy on Comets*, 36–39; also Drake, *Galileo at Work*, 271). He seems not to have abandoned his skepticism in the *Dialogue Concerning the Two Chief World Systems*, where his spokesman Salviati, after first asserting that "excellent astronomers have observed many comets generated and dissipated in places above the lunar orbit, besides the two new stars of 1572 and 1604, which were indisputably beyond all the planets" (Drake tr., 51), goes on to explain (ibid., 52) that:

"As far as the comets are concerned I, for my part, care little whether they are generated below or above the moon, nor have I ever set much store by Tycho's verbosity. Neither do I feel any reluctance to believe that their matter is elemental, and that they may rise as they please without encountering any obstacle from the impenetrability of the Peripatetic heavens, which I hold to be more tenuous, yielding, and subtle than our air. And as to the calculation of parallaxes, in the first place I doubt whether comets are subject to parallax; besides the inconstancy of the observations upon which they have been computed renders me equally suspicious of both his opinions and his adversary's. . . ."

In this passage, Galileo seems to believe that

comets are formed from vapors of terrestrial origin, which could however rise into the heavens, since the latter were sufficiently tenuous to be penetrated. But he does not assume that they actually rise into the heavens because he (1) doubts whether they are subject to parallax, presumably because, as in the *Discourse on Comets*, he was still unconvinced that they were real bodies, and (2) because even if they were subject to parallax, the computations of parallaxes is unreliable. Except for the assumption of a tenuous and permeable heaven and the possibility that the constituent vapors of comets might rise into the heaven, Galileo's opinions were not uncommon among scholastics, who also took advantage of the uncertainties of parallax measurements and who also believed, with Aristotle, that comets were formed from sublunar vapors.

32. Aversa, ibid., 89, col. 2–90, col. 1.

33. Aversa's shift from rare and dense to transparent and opaque was seemingly prompted by his belief in the solidity of the celestial spheres and by a comparison of crystal and wood. Although crystal is quite dense it is not opaque but transparent, whereas wood, which is more opaque than crystal, is less dense. The transparency of the heaven is thus a result of its great density and not of its rarity. For Aversa, then, the traditional opinion that stars are denser portions of celestial ether which are capable of reflecting light and becoming visible is untenable. In terms of the analogy between crystal and wood, the opposites dense and rare cannot explain the appearance of planets and stars as dense clusters of ether and the transparency of the celestial spheres as the rarer parts of the heavens. By substituting transparent and opaque, however, Aversa associated the former with the invisible celestial spheres and the latter with the visible planets and stars.

34. *Almagestum novum astronomiam veterem novamque complectens observationibus aliorum et propriis novisque theorematibus, problematibus ac tabulis promotam; in tres tomos distributam* . . . (Bologna, 1651), pars posterior, 238, col. 1. Only the first volume, in two parts, appeared. For Melchior Cornaeus, see *Curriculum philosophiae peripateticae, uti hoc tempore in scholis decurri solet* . . . *auctore Melchiore Cornaeo, Soc. Iesu, SS. Theologiae doctore eiusdemque in alma universitate Herbipolensi professore ordinario* (Würzburg, 1657), 489; for George de Rhodes, see *R. P. Georgii de Rhodes Avenionensis, e Societatis Iesu, Philosophia peripatetica ad veram Aristotelis mentem libris quatuor digesta et disputata* . . . (Lyon, 1671), 278–81.

35. Ibid., 239, col. 1.

36. Ibid., 233, col. 2; 236, cols. 1–2.

37. In his *Astronomiae Instauratae Mechanica* of 1598, Tycho declared that the "whole heaven is most transparent and fluid and is not filled with hard and real orbs" ("totum caelum limpidissimum et liquidissimum esse, nullisque duris et realibus orbibus refertum"). The *Mechanica* has been reprinted in the modern edition of Tycho's works. See *Ty-*

chonis Brahe Dani Opera omnia, J. L. E. Dreyer, ed., 15 vols. (Copenhagen, 1913–1929), 5: 117. For some years before he wrote the lines cited above, Tycho had denied the existence of solid spheres in both published works and in correspondence. See *Opera* 3 (*Progymnasmata*; although published in 1602, most of it was written long before): 78, 90–91, 111, 151; 4 (*De mundi aetherei recentioribus phaenomenis*): 159, 222ff; 6 (correspondence with Rothmann): 88, 140, 148, 187; 7 (general correspondence): 130, 163, 229, 260, 267, 293); 8: 45, 206, 208. For the references to Tycho's works, I am grateful to my colleague, Victor E. Thoren. Donahue (*Dissolution of the Celestial Spheres*, 63) explains that Tycho had already "read and substantially agreed with Cardan's comet theory [which located comets in the celestial region], and he also comments favourably upon the idea, which he attributes to Paracelsus, that the heavens are filled with fire. At the very least, this shows that his investigation of the parallax of the 1577 comet was inspired by a philosophical viewpoint which was not in the Aristotelian mainstream." The bracketed phrase is mine. A contrasting hypothesis fits the situation just as well. Having discovered a parallax that would place the comet of 1577 above the moon, Tycho then sought support for what was still a daring opinion in the sixteenth century.

38. See Roderigo de Arriaga, *Cursus philosophicus* (Antwerp, 1632), 503, col. 1; Franciscus Bonae Spei, *Commentarii tres in universam Aristotelis philosophiam: commentarius tertius in libros De coelo, De generatione et corruptione, De anima, et Metaphysicam Aristotelis* (Brussels, 1652), 13, col. 2–14, col. 1; and Franciscus de Oviedo, *Integer cursus philosophicus ad unum redactus, in Summulas, Logicam, Physicam, De caelo, De generatione, De anima, et Metaphysicam distributus* (2 vols.; Lyon, 1640), vol. 1, 468, col. 2–469, col. 1.

39. We have already seen this since Riccioli assumed that the sphere of the fixed stars was congealed water and the rest of the heaven was a fiery fluid.

40. For a brief discussion and references, see Grant, "In Defense of the Earth's Centrality and Immobility," 13.

41. Only a skeletal summary is given here of a detailed discussion in Grant, "In Defense of the Earth's Centrality and Immobility," 22–31. Aristotle had argued (*Meterologica* 2.2.354b. 23ff.) that the four elements were arranged concentrically from the center outward to the concave surface of the lunar sphere in the order: earth, water, air, and fire. He was, however, aware that this scheme was not fully realized in nature because dry land extended above the waters and fire could be seen on the earth's surface.

42. In the fourteenth century, John Buridan provided an accurate description of the terraqueous sphere only to reject it. See *Iohannis Buridani Quaestiones super libris quattuor De caelo et mundo*, ed. Ernest A. Moody (Cambridge, Mass.: Mediaeval Academy of America, 1942), 157. For a translation of the rel-

evant passage, see Edward Grant, *A Source Book in Medieval Science* (Cambridge, Mass.: Harvard University Press, 1974), 622.

43. *Nicholas Copernicus On the Revolutions*, ed. Jerzy Dobrycki, translation and commentary by Edward Rosen (Baltimore: The Johns Hopkins University Press, 1978), bk. 1, ch. 3 ("How Earth Forms a Single Sphere with Water"), 9.

44. For Clavius's discussion, see *Christophori Clavii Bambergensis ex Societate Iesu in Sphaeram Iohannis de Sacro Bosco Commentarius* (4th ed.; Lyon, 1593), 133–51 ("whether earth and water form one globe . . ."). Judging by the bibliography in Carlos Sommervogel, S. J., *Bibliothèque de la Compagnie de Jésus* (12 vols.; Brussels/Paris, 1890–1911), vol. 2, cols. 1212–1213, Clavius's *Commentary on the Sphere of Sacrobosco* went through at least five editions and fourteen printings.

45. See Edward Grant, *Much Ado About Nothing: Theories of Space and Vacuum from the Middle Ages to the Scientific Revolution* (Cambridge: Cambridge University Press, 1981), 116–144 (for medieval arguments) and 152–181 (for sixteenth and seventeenth century scholastics, among whom were Franciscus Suarez and Bartholomew Amicus).

46. During the Middle Ages, many accepted the real existence of eccentric and/or epicyclic spheres (for example, see Pierre d'Ailly's *14 Quaestiones* [i.e. *14 Questions on the Sphere of Sacrobosco*] in *Spherae Tractatus Ioannis De Sacro Busto Anglici viri clariss.; Gerardi Cremonensis Theoricae planetarum; . . . Alpetragii Arabi Theorica planetarum nuperrime latinis mandata literis a Calo Calonymous Hebreo Neopolitano, ubi nititur salvare apparentias in motibus planetarum absque eccentricis et epicyclis* (Venice, 1531), question 13 ("whether, in order to save the appearances, it is necessary to assume eccentric and epicyclic circles"), fols. 163v–164v. For seventeenth-century defenses of eccentrics and epicycles, see Clavius, *In Sphaeram Iohannis de Sacro Bosco Commentarius* (Lyon, 1593), 499–525 ("By what appearances have eccentrics and epicycles been found in the heavens by astronomers") and Bartholomew Amicus, *De caelo*, 265, col. 1–270, col. 2 ("whether eccentrics and epicycles must be assumed").

47. For the identification of celestial and terrestrial matter by Aegidius Romanus and William Ockham, see Edward Grant, "Celestial Matter: A Medieval and Galilean Cosmological Problem," *Journal of Medieval and Renaissance Studies*, 13, nr. 2 (1983), 165–172. Although conceived rather differently, Franciscus Bonae Spei, and others, made the same identification in the seventeenth century (see Franciscus Bonae Spei, *Commentarii tres in universam Aristotelis philosophiam: commentarius tertius*, 9, col. 2–10, col. 1.

48. A summary of these arguments appears in Edward Grant, "Bradwardine and Galileo: Equality of Velocities in the Void," *Archive for History of Exact Sciences*, 2, nr. 4 (1965), 355–364.

49. For example, the following departures from Aristotle

were proposed: (1) that it was not absurd that unequal but homogeneous bodies would fall with equal speeds in a vacuum (see Grant, "Bradwardine and Galileo," 344–355; (2) that bodies are moved violently by impressed forces (or impetus) rather than by air (see Marshall Clagett, *The Science of Mechanics in the Middle Ages* [Madison, Wis.: University of Wisconsin Press, 1959], chs. 8, 9, 505–582); and (3) that heavy and light bodies, and the places associated with them, are relative (see *Nicole Oresme: Le Livre du ciel et du monde*, edited by Albert D. Menut and Alexander J. Denomy; translated with an introduction by Albert D. Menut (Madison, Wis.: University of Wisconsin Press, 1968), 71, 173.

50. See *Le opere di Galileo Galilei*, 10: 68.

51. No plausible evidence has yet appeared to suggest that fourteenth-century discussions of the earth's possible axial rotation by John Buridan and Nicole Oresme had any influence on Copernicus (for the texts, see Clagett, *The Science of Mechanics in the Middle Ages*, 583–609 and Grant, *A Source Book in Medieval Science*, 500–510).

52. The arguments are described in Grant, "In Defense of the Earth's Centrality and Immobility."

53. See Jones, "The Geoheliocentric Planetary System," 286.

54. See Riccioli, *Almagestum novum*, pars posterior, 469, col. 1. Because most scholastics in the seventeenth century believed that animate beings, however lowly (thus including even wasps and flies), were nobler than the inanimate planets and stars, Riccioli inferred that the earth on which they lived must also be nobler than the sun, which was often considered the noblest planet. I have treated this issue at length in a forthcoming article, ("Celestial Perfection From the Middle Ages to the Late Seventeenth Century") that will appear in a festschrift volume (Cambridge University Press) edited by Margaret J. Osler and Paul L. Farber; see also Grant, "In Defense of the Earth's Centrality and Immobility," 59.

55. I have described the capaciousness of early modern Aristotelianism in my article, "Aristotelianism and the Longevity of the Medieval World View," *History of Science*, 16 (1978), especially 100–101.

56. Some have already been mentioned, for example, the reality of eccentric and epicyclic spheres, impetus theory, the identification of celestial and terrestrial matter, and the existence of an infinite extracosmic void space.

57. That scholastics rarely drew potentially devastating consequences from their sometimes innovative ideas is perhaps attributable to the nature of the *questiones* form of scholastic literature, which emphasized the independent question and effectively "prevented any larger synthesis that might have forced a major overhaul or reconstitution of Aristotelian cosmology." This "atomization of Aristotle's physical treatises resulted in an intellectual flotsam and jetsam of unrelated questions which actually concealed grave inconsistencies and discrepancies" (Grant,

"Aristotelianism and the Longevity of the Medieval World View," 98–99).

58. See Andreas Cesalpino, *Peripateticarum quaestionum libri quinque* (Venice: apud Iuntas, 1571), bk. 3, question 4, fols. 53r–59v; and for a summary of Cesalpino's arguments, Grant, "In Defense of the Earth's Centrality and Immobility," 6–8.

59. "Si Aristoteles hodie viveret et quas modo nos in sole alterationem et conflagrationes deprehendimus, videret, absque dubio mutata sententia nobiscum faceret. Idem sane est de planeteis, quos Philosophus septenis plures non agnoscit. At nos hoc tempore opera telescopii (quo ille caruit) plures omnino esse certo scimus." Corneaus, *Curriculum philosophiae peripateticae*, 503. Through his spokesman, Salviati, Galileo had earlier said much the same thing: "I declare that we do have in our age new events and observations such that if Aristotle were now alive, I have no doubt he would change his opinion" (*Dialogue Concerning the Two Chief World Systems*, Drake tr., 50).

60. "Respondeo authoritatem Aristotelis non ita attendi quia in libris *De coelo* pluries erravit." Franciscus Bonae Spei, *Commentarii tres in universam Aristotelis philosophiam: commentarius tertius*, 14, col. 2.

61. Occasionally, the process worked the other way, with a nonscholastic scientific author retaining an important piece of Aristotelian cosmology. Thus Otto von Guericke, a confirmed Copernican (*Experimenta nova*, 218, col. 1, where he says: "Ergo Copernicanum Systema est verum et alteri praeferendum") insisted that the planets moved with perfect regularity and therefore did not vary their distances from the earth. As he explained it (ibid., 166, col. 1):

"Indeed it is true that we see the sun and, other things being equal, the moon now greater and now smaller. But this is not because of an approach and withdrawal of these bodies toward [and away from] the earth, but [because of] air, which, on account of its diverse higher or wetter constitution, or because of its greater or lesser depth, causes different appearances."

By his belief in perfect circular motions for the planets and denial of any variation in their distances, Von Guericke, though a Copernican, retained one of the most basic of Aristotle's cosmological tenets. In this sense, he seems a purer Aristotelian than medieval and contemporary scholastics, very few of whom would have denied the real variation of planetary distances.

Kuhn, Paradigms, and Astronomy:

Astronomy as a Case Study of Kuhnian Paradigms

J. Bruce Brackenridge

I. Introduction

Thomas Kuhn's *The Structure of Scientific Revolutions* is a small book published in 1962 by a young physicist turned historian of science turned philospher of science.[1] In the twenty years following its publication it has sold more than half a million copies of its two English editions plus translations into eighteen languages. The *Science Citation Index* for 1981 lists nearly one hundred articles published in that year alone that cite *SSR*. The *Social Science Citation Index* for the same year lists more than three times that amount.[2] It has been reviewed in a variety of scholarly journals[3] and has been the subject of a very large number of scholarly articles.[4] But its scholarly success should not imply that it was or is universally accepted as a new dogma of "what science is." Quite the contrary, it is enthusiastically acclaimed by some, vigorously opposed by others, but rarely is it ignored. What is clear, however, is that it offers to opponents and supporters alike a fresh, incisive, and meaningful view of the complex activity called science.

Perhaps Kuhn's initial appearance of "freshness" came from his lack of professional training in the humanities. The work was written after he finished his formal training in physics and before being indoctrinated into the formal language of the historian and philosopher of science. As one reviewer put it, "It is a tribute to the power of Kuhn's mind that, instead of grasping

other's [sic] answers, he created his own." Clearly, the scientific activity described and the terms employed are familiar to the working physicist. In contrast to Popper's "falsification" and Lakatos's "competing programmes," the average physicist can recognize Kuhn's analogy of "normal science" with "puzzle solving." His use of "anomaly" to identify a particularly difficult puzzle that is not yet solved fits into many textbook descriptions of scientific activity. "Crisis" as a state that may be produced by extremely persistent anomalies (black-body radiation, for example) and the ensuing "scientific revolution" that bends established rules (Quantum postulates) are all familiar to the instructor in physics. Even Kuhn's elusive concept of a "paradigm" strikes a sympathetic chord with many physicists, particularly in the more restricted form of a "set of exemplars."

The comments on Kuhn's work range from "brilliant new insights" to a "brilliant wrong idea." But brilliant or banal, Kuhn has become a factor to deal with for anyone with an interest in the structure of science. It may be, as some have claimed, that "Kuhn's overall idea about science is wrong—and many of those who think it is right have simply misunderstood it." I shall argue, however, that many of those who are most vocal in attacking Kuhn have not fully understood an important aspect of his views. In any event, there is ample support for reading the work, right or wrong. The review in *The Chronicle of Higher Education* [note 2]

concludes with the following appraisal: "Across the board, however, professors agree that it is invaluable as a textbook, and as a starting point for any discussion of the philosophy of science. . . . Nearly everyone agrees that there are countless valuable insights in his book."

The goal of science is to create a model of the world that scientists can understand. The goal of philosophy of science is to create a model of science that philosophers can understand. It is Kuhn's intent in *SSR* to offer an alternative to the traditional Baconian view of science as an inductive process that moves from naive facts to sophisticated hypothesis in some natural fashion. In what follows, I neither defend nor attack Kuhn's analysis of the structure of science and its progress. Nor do I offer any evaluation of it except to applaud it as an attempt to give an alternative view of the complex activity that is science. Rather, I use astronomy as a case study to present my views of Kuhn's views of progress in science.

II. The Senses of "Paradigm"

The key to understanding Kuhn is a biographical one. And no one understands it better than Kuhn himself. There are constant references to "autobiographical information" as he attempts to develop his thesis. He was first trained as a physicist, and from an analysis of this training he was to gain his first original insights for his model of Normal Science. Then, after completing his Ph.D. in physics, he had the opportunity to spend three years as a Junior Fellow at the Society of Fellows of Harvard University, and it was here that, as Kuhn puts it, "James B. Conant . . . first introduced me to the history of science and thus . . . initiated the transformation in my conception of the nature of scientific advance." This interest in the history of science gave rise in 1957 to his book *The Copernican Revolution,* and he entered the lists of professional philosophers of sci-

ence in 1962 with the publication of his book *The Structure of Scientific Revolutions.* It is because of this precise sequence of interests, first a practicing physicist, then a historian of science, and finally a philosopher of science, that Kuhn has been capable of new insights generally denied philosophers not trained in physics. The price he had to pay, however, was that he has had to battle to achieve a sense of historical perspective that normally is part of the training of the humanist, but not of the scientist. The final combination of these two elements, one "obvious" to the trained physicist and the other "obvious" to the trained historian, are employed by Kuhn in his key concept of a "paradigm." It is at once the solution to and the source of the problems that Kuhn faces from his multiple critics.

The concept of paradigms proved to be the missing element I [Kuhn] required in order to write the book [*SSR*]. . . . Unfortunately, in that process, paradigms took on a life of their own. . . . Having begun simply as exemplary problem solutions [that aspect obvious to the physicist], they expanded their empire to include first, the classic books in which these accepted examples initially appeared and, finally, the entire global set of commitments shared by the members of a particular scientific community [that aspect obvious to the historian]. That more global use of the term is the only one most readers of the book have recognized, and the inevitable result has been confusion. . . . Clearly, I have made unnecessary difficulties for many readers.[5]

Despite the difficulty inherent in understanding the concept of paradigms as set forth in *SSR,* Kuhn defends their importance. In an essay entitled, "Second Thoughts on Paradigm," he states, "However imperfectly I [Kuhn] understood paradigms when I wrote the book, I still think them worth much attention."[6]

The inherent confusion in Kuhn's initial discussion of paradigms is set forth in an essay by Margaret Masterman entitled "The Nature of a Paradigm," in which she takes

to task Kuhn's multiple use of the word paradigm.[7] Masterman's essay was not in the nature of a controversial commentary; quite the contrary, she is very supportive of Kuhn's work. In her opening line she stated, "The purpose of this paper is to elucidate T. S. Kuhn's conception of a paradigm; and it is written on the assumption that T. S. Kuhn is one of the outstanding philosophers of our time." She admitted, though, that "Kuhn, of course, with that quasipoetic style of his, makes paradigm-elucidation genuinely difficult for the superficial reader."[8] To demonstrate the challenge of understanding Kuhn's "poetry," she added that "on my counting, he uses 'paradigm' in not less than twenty-one different senses," and she then identified all twenty-one. She then attempted masterfully to condense all twenty-one into three main categories.[9]

In a postscript added to his second edition of *SSR*, Kuhn refers directly to Masterman's analytical index of the different senses in which the term "paradigm" is used in the body of his text, but he tacitly rejects her classification schemes.[10] In what may be taken to be a masterful understatement he claims "that most of the differences [in the way in which the term 'paradigm' is used] are, I now think, due to stylistic inconsistencies . . . and they can be eliminated with relative ease."[11] In this new edition, however, he does not attempt that "editorial" task of removing the "stylistic inconsistencies" in the body of the essay, but in a postscript he does clarify how it could be done. But with that editorial work done, Kuhn states, "two very different usages of the term [paradigm] would remain, and they require separation. Until the term [paradigm] can be freed from its current implications, it will avoid confusion to adopt another [term for it]."[12] He adopts in fact two new terms, one for each of the distinct uses of the term paradigm that he is to identify: the "more global use" to be called a "disciplinary matrix" and the more restricted use to be called a "set of

exemplars." It is this global sense of paradigm, the disciplinary matrix, that most readers have recognized. It is the more restricted sense, the set of exemplars, that, despite its primary and concrete nature, has escaped most historians and philosophers who have commented upon Kuhn's work.

This restricted sense of paradigm is as obvious to the physicist as it is elusive to the humanist. Kuhn's genius was to see how it could serve to give insights into the larger structure of science. Put very simply, physics is what physicists do and physicists do what they are taught to do. Moreover, physicists are taught from textbooks. And it was an attempt to understand this textbook tradition of physics that led Kuhn to his initial insights into the entire structure of physics. He described this attempt in his preface to his collected essays.

At that time I [Kuhn] conceived normal science as the result of a consensus among members of a scientific community. Difficulties arose, however, when I tried to specify that consensus by enumerating the elements about which members of a given community supposedly agree. . . . I had to attribute to them agreement about the defining characteristics of such quasi-theoretical terms as 'force' and 'mass', or 'mixture' and 'compound'. But experience, both as scientist and historian, suggested that such definitions were seldom taught. . . . What I finally realized early in 1959 was that no consensus of quite that kind was required. If scientists were not taught definitions, they were taught standard ways to solve selected problems in which terms like 'force' or 'compound' figured. If they accepted a sufficient set of these standard examples, they could model their own subsequent research on them without needing to agree about which set of characteristics of these examples made them standard. . . . That procedure seemed very close to the one by which students of language learn to conjugate verbs and decline nouns and adjectives. . . . The usual English word for the standard examples employed in language teaching is 'paradigms,' and my ex-

tension of that term to standard scientific problems like the inclined plane and conical pendulum did it no apparent violence.[13]

The importance of such "standard sets of examples" is clear to every instructor in physics. When students report that "they have read the chapter of their text, understood it perfectly, but nonetheless had difficulty solving the problems at the end of the chapter,"[14] the temptation for the instructor is to smile. For it is clear that the "understanding" resides in the ability to produce problem solutions, not in the "reading of the chapter." One need only look at the typical examination in physics to realize that the payoff is in the problem replication and not in the demonstration of having read and understood (in a literal sense) the chapter. And it was the realization of how important this aspect of the education of the physicist was, that led Kuhn to his first use of the word "paradigm" (literally, he says it means "standard examples"). "[Textbooks] exhibit concrete problem solutions that the profession has come to accept as paradigms."[15] And in learning to produce such solutions, students learn much more than is, or can be, stated explicitly in the chapter. They have to learn to "think physically," whatever that means.

This central element, however, is described by Kuhn as "the most novel and least understood aspect of this book." As an example of one of the few who does understand what he means by this central element, Kuhn points to the work of Wolfgang Stegmüller:

Though both senses [of paradigm] seem to me important, they do need to be distinguished and the word 'paradigm' is appropriate only to the first [exemplars]. Clearly I have made unnecessary difficulties for many readers. . . . Wolfgang Stegmüller has been especially successful in finding his way through these difficulties. . . . He discusses three senses of the term, and the second, his Class II, captures precisely my original intent [exemplars].[16]

This class II is described by Stegmüller as "the set I of intended applications determined by paradigmatic examples."[17] Without attempting to develop the careful and complex analysis of Stegmüller, which Kuhn applauds,[18] I wish merely to emphasize that it is a "set of exemplars" (plural) that Kuhn identifies as capturing his original intent and that he stresses the need to distinguish between the two "senses" of paradigm.

An example of one of the many who fail to make such a distinction and thus fail to understand Kuhn's original intent is a reviewer of *The Essential Tension.* He claims that central to Kuhn is the hermeneutic problem of understanding scientific documents of an earlier period. Further, he claims that the implied answer given by Kuhn is as follows:

Basically, and cutting away most of the philosophical verbiage which Kuhn himself admits to be superfluous in his "Second Thoughts on Paradigms", one goes to scientific textbooks of the period under study and discovers what the "consensus" of scientists is on any given matter. Then, and only then, can one read a scientific document of that period with some security.[19]

But Kuhn has pointed out that no such verbal or formulaic "consensus" is directly articulated in textbooks (see note 13). The entire point of paradigm in the restricted sense (set of exemplars) was to speak to the absence of such a clear consensus. But the reviewer has chosen to ignore such distinctions, and he continues throughout the remainder of the review to flail away at paradigm as the "consensus found in textbooks." The reviewer has failed to understand the importance Kuhn places on the role of the set of exemplars in textbooks.

Why has this "restricted" sense of paradigm been so completely overlooked by Kuhn's commentators? One answer may be that they are not teaching introductory science courses and hence are not aware of the importance of concrete problem replication

in textbooks of science. It follows that they would thus be less likely to grasp the subtle sense in which, for Kuhn, the textbook and its sets of exemplars (the restricted sense of paradigm) reflects the nature of the disciplinary matrix (the global sense of paradigm). Put most simply, there are important aspects in the teaching and practice of science that cannot be articulated literally but that nevertheless play important roles. Kuhn's failure to find a consensus in the descriptive material in scientific textbooks led him to his restrictive sense of paradigm, and this discovery then led to the more global sense, the disciplinary matrix.

Moreover, Kuhn may still be guilty in his postscript of the "stylistic inconsistencies" that he acknowledges in his original essay. Further confusion concerning the term "exemplar" occurs when it is seen to be a single major work (such as Newton's *Principia*) or as a single problem solution (such as the planetary ellipses, Proposition XI, Book I) after which all other solutions are somehow imperfectly modeled (see footnote 13). And Kuhn's rather indiscriminate use of the singular and plural forms of paradigm for "exemplars" or for "sets of exemplars" adds to this confusion. In his attempt to eliminate "stylistic inconsistencies" he would have been well advised to be consistent in identifying the central element of the disciplinary matrix by a single phrase, and I suggest that "set of exemplars" would be most appropriate.

B. Paradigm as a "Disciplinary Matrix"

If the more restricted sense of paradigm (set of exemplars) came from Kuhn's initial training as a physicist, then this more global sense (disciplinary matrix) came from his subsequent training as a historian. As another reviewer of Kuhn's collected essays puts it:

One of the more striking aspects of Kuhn's work is how much of it is shaped by his early experiences as a practising historian of science. What we find above all is the influence of his discovery in 1947 of "the connected rudiments of an alternative way of reading (historical) texts," according to which in order to understand why, say, Aristotelian physicists said what they did, it is necessary "to some extent (to learn) to think like one" (p. xi and p. xii). This discovery which—as Kuhn himself notes (p. xiii)—is commonplace among historians, was for him nothing short of "decisive" (p. xii), influencing many of his views about the correct way of practising history of science, the origins of modern science and the nature of scientific change.[20]

In order to "think like" an Aristotelian physicist, the historian of science must somehow be able to shift from his contemporary world view to that of the Aristotelian, or at least to be aware of and responsive to such differences. It is not part of the training of the contemporary physicist to be aware that such differences exist and are important. Quite the contrary, modern textbooks in physics, Kuhn would claim, are written to obscure such differences and to ascribe to the discipline a linear development. Primary sources such as Newton's *Principia* are not read (for the work is, in fact, quite incomprehensible to a contemporary physicist). Instead, the textbook presents the material in the most efficient way and gives the source credit for what it "should" have said. It rarely seems important in understanding contemporary science to try to "think like" Newton, much less like Aristotle. It was as a historian, however, in the attempt to understand such world views, i.e., such global sets of commitments, that Kuhn was led to his conception of the larger sense of paradigm, the disciplinary matrix.

If the problem of understanding Kuhn's original meaning for paradigm as "a set of exemplars" is that it is so restrictive, then the problem of understanding his meaning for paradigm as "a disciplinary matrix" is that it is so global. It is called " 'disciplinary' because it refers to the common possession of the practitioners of a particular discipline;

'matrix' because it is composed of ordered elements of various sorts, each requiring further specification." Kuhn gives three of the "ordered elements" of the matrix: (1) symbolic generalization, (2) metaphysical parts, and (3) shared values. This listing does not constitute "an exhaustive list," however, but contains simply "the main sorts of components of a disciplinary matrix." Further, these elements "require further specification" and perhaps may themselves contain subsections.

It is essential to note the correspondence between paradigm as a set of exemplars and paradigm as a disciplinary matrix relative to their *intrinsic inability to be fully articulated.* Just as it is impossible to articulate all the elements of the disciplinary matrix or even to spell out in complete detail any given element, so it is impossible within a chapter of a textbook to articulate all that is essential to understanding the topic under discussion. One must rely on the set of exemplars that appears as problem sets at the end of the chapter to communicate by example that which cannot be literally articulated.

C. PARADIGM AS A MATRIX ELEMENT

Kuhn is thus hopeful that he will have eliminated much of the confusion and unnecessary difficulties that arise for many readers concerning the meaning of "paradigm" by distinguishing between the two senses of the term: "sets of exemplars" and "disciplinary matrix." Unfortunately, in *SSR* Kuhn also refers to a third item as a "paradigm": a single element of a disciplinary matrix other than the unique central element that is the set of exemplars. These references occur in the original edition, before the distinction between exemplars and a matrix is made, thus one can understand the source of the additional confusion. Nevertheless, the reader has in fact *three* choices for the term "paradigm" each time it appears in the body of the original text, and the choice can

be made only within the context of a given usage. But a choice must be made if confusion is to be avoided.[21]

Matrix Elements

There is, however, still more to be gained from further inspection of the individual elements of the disciplinary matrix that Kuhn discusses. Clearly these are examples of elements that can be articulated, and as such they are closely affiliated with the "rules" that guide scientific behavior. It is instructive to look more closely at the three elements of the disciplinary matrix given by Kuhn and then at his examples of the "rules" that can be abstracted from them.

I. *Symbolic generalizations:* The first element of the matrix is identified is labeled "symbolic generalizations" and Newton's second law, $f = ma$, is given as a prime example.[22] Two functions of this element are given to indicate the kind of "further specification" that is useful. First, "these generalizations look like laws of nature": that is, they tell something about the behavior of defined symbols. But they "simultaneously serve a second function . . . as definitions of some of the symbols they deploy."

II. *Metaphysical parts:* The second element of the matrix can be called "metaphysical parts," or at least, Kuhn claims, that is the rubric that has been used by commentators on his work.[23] He describes these shared commitments as "beliefs in particular models" and gives as one of a number of examples the belief that "all perceptible phenomena are due to the interaction of qualitatively neutral atoms in the void, or, alternatively, to matter and force, or to fields."

III. *Shared values:* The third element of the matrix is described as "shared values."[24] This element, like all elements in a particular matrix, is shared by members of the discipline. But, according to Kuhn, particular values are more often shared by different disciplines

than are either symbolic generalizations or models. A prime example might be "values held concerning predictions: they should be accurate; quantitative predictions are preferable to qualitative ones," etc.

Rules and Matrix Elements

Further insight into what Kuhn means by the disciplinary matrix can be obtained from his discussion of "rules," a term whose relationship to normal science and paradigms is the topic of two chapters in *SSR*. "Rules" are defined as "isolable elements, explicit or implicit, [that] members of the community may have abstracted from their more global paradigms."[25] In terms of the previous discussion of disciplinary matrix, rules are those portions of the disciplinary matrix that can be literally articulated.

The first category of rules is identified as "generalizations" and stems directly from the element of the disciplinary matrix called "symbolic generalization."[26] Newton's second law appears as the example in both descriptions. The second category of rules is entitled "quasi-metaphysical commitments" and is directly related to the element of the disciplinary matrix called "metaphysical parts."[27] The third category of rules listed by Kuhn entails "still a higher level . . . a set of commitments without which no man is a scientist."[28] This set of rules is related to the third element of the disciplinary matrix called "shared values" and it is important since it is this matrix element that appears to survive during revolutions from one paradigm to another.

Kuhn further provides a fourth category of rules and it indicates a fourth element of the disciplinary matrix. At a lower and more concrete level than "symbolic generalizations," there exists in Kuhn's categorizing of rules a commitment to preferred types of instrumentation and to the ways in which accepted instruments may be legitimately employed.[29] The corresponding element of the

disciplinary matrix could be called "instrumental commitments."

One could go on, as Kuhn has indicated, filling out matrix elements in a very general way, perhaps some even as diffuse as "political commitments." Regardless of how carefully one attempted to set forth such elements, however, some could not be articulated. Just as the scientist as educator must rely on the sets of exemplars to communicate aspects of science that cannot be written down in the textbook, so the scientist as researcher must rely on rules that cannot be fully articulated to guide research and behavior.

III. ASTRONOMY AS A "CONSTELLATION OF GROUP COMMITMENT"

One could continue to try to expand the disciplinary matrix by seeking out other general examples of elements. It is more productive, however, to select a given scientific discipline and to inspect it for the given Kuhnian elements. A logical choice for the case study is astronomy. In a 1976 essay entitled "Mathematical versus Experimental Traditions," Kuhn asks the question, "Among the large number of topics now included in the physical sciences, which ones were already in antiquity foci for the continuing activity of specialists? The list is extremely short. Astronomy is its oldest and most developed component."[30] The other "classical" sciences on his short list include only statics and optics. The other areas that we now designate as physical sciences arose during the seventeenth century and Kuhn refers to them as the "Baconian" or "Experimental" sciences. Thus, because of its long history, and because it lends itself most easily to Kuhn's analysis (see Stegmüller, note 17 and 18), astronomy is selected as the case study. It played such a role for Kuhn, since he published *The Copernican Revolution* only five years before he published *SSR*.

The history of planetary astronomy may

be divided into three major areas: Babylonian arithmetical astronomy, Greek geometrical astronomy, and Newtonian analytical astronomy. It is useful to concentrate upon a specific problem, such as the analysis of the motion of the planet Mars. The general problem of planetary motion was the single most important topic in astronomy from the nineteenth century B.C. to the nineteenth century A.D. The solution to the specific problem of the description of the motion of Mars, in fact, was the watershed between Greek geometrical and Newtonian analytical astronomy.

This third and final section explores the correspondence between the specific practices of astronomy in a given period and Kuhn's definition of the general structure of science. The three redefinitions of paradigm (set of exemplars, disciplinary matrix, and individual matrix elements) will be elucidated by specific and detailed examples, and Kuhn's use of "anomaly" and "counterinstance" will be explicated.

In terms of Kuhn's analogy of normal science as a puzzle-solving activity, an anomaly is a puzzle that science has not yet been able to solve, but one that it expects to solve. Until such a solution is found, the scientist must face "the recognition that nature has somehow violated the paradigm-induced expectations that govern normal science."[31] A counterinstance in the vocabulary of philosophy of science is an anomaly.[32] For the philosopher it is an example of an item that is also counter "to a prevalent epistemological theory."[33] But "normal" scientists do not treat anomalies as counterinstances.[34] What "normal" scientists will do, however, is to "devise numerous articulations and *ad hoc* modifications of their theory [elements of their disciplinary matrix] in order to eliminate any apparent conflict."[35] The anomaly is seen by scientists as a counterinstance only when all such paradigmatic adjustments fail and when a solution is found that requires a major revision in the rules of puzzle-solving,

i.e., that which Kuhn calls a revolution or paradigm-switch. A major anomaly for astronomers before the eighteenth century was the puzzle that was the description of the motion of the planet Mars. The mandated major revision of the rules required astronomers to set aside the belief that the motion of planets could be described only by combinations of perfect circles. This puzzle was finally solved by Newton in 1687 when he was able to derive Kepler's planetary ellipse of 1609.

By the early eighteenth century, Western astronomy was centered about a single work, *The Principia* of Sir Isaac Newton, just as western astronomy before the seventeenth century was centered on another single work, *The Almagest* of Ptolemy. Kuhn claims that before the time of scientific textbooks and journals, such classic works functioned in their stead "to attract an enduring group of adherents away from competing modes of scientific activity [and] . . . to leave all sorts of problems for the redefined group of practitioners to resolve."[36] Kuhn then goes on to say that "achievements that share these two characteristics I shall henceforth refer to as 'paradigms'."[37] It is clear now from the postscript in the second edition of *SSR* that the concrete problem-solutions within each work are the paradigm in the restricted sense (now called a "set of exemplars"), and further that the symbolic generalizations, models, and values, along with all other shared commitments that the work reveals, are also the paradigm in the global sense (now called the "disciplinary matrix"). There are many case studies that could be selected but astronomy is of particular interest because a single dominant source does exist for astronomy in each of two widely separated periods of scientific activity.

A. NEWTONIAN ANALYTICAL ASTRONOMY

Newtonian analytical astronomy provides a clear example of what Kuhn means by a

disciplinary matrix. The central element of this disciplinary matrix of the "enduring group of adherents" attracted to astronomy by the *Principia* is the Kuhnian set of exemplars that are to be found in the problems, answers, and demonstrations contained within this work. The *Principia* is, in fact, almost entirely a collection of specific problems and specific methods for obtaining their specific solutions. There is an introduction of 19 pages containing definitions and laws of motion, followed by the 245 pages of Books I and II, containing 58 problems and their detailed solutions and 91 theorems and their proofs. Book III opens with two pages of rules of reasoning and closes with two pages of a general scholium, but the intervening 97 pages contain 22 problems and their solutions, 20 theorems and their proofs, and six statements on phenomena. The road to articulation of Newtonian astronomy is clear. Begin at the center of the disciplinary matrix with the concrete problem solutions in the *Principia* that constitute the basic set of exemplars and then attempt to articulate as many of the other elements of the disciplinary matrix as possible. In what follows, one particular concrete problem solution, the motion of the planet Mars, is selected and Newton's solution is analyzed in three steps.

The Central Element: The "Set of Exemplars"

The first step addresses the general problem of the idealized motion of any single isolated planet about a fixed sun. Newton assumed that the motion of such an ideal planet will be an ellipse with the sun located at one focus. Further the planet will move at a rate such that a line drawn from the sun at the focus of the ellipse to the planet moving on the curve of the ellipse will sweep out equal areas in equal times. Such planetary motion has been demonstrated by Kepler to be valid for Mars within certain carefully prescribed limits. From this knowledge of the

path and rate of the hypothetical planet, Newton derived the nature of the force that must exist between the sun and the planet. Employed in this analysis is an embryonic form of the relationship $f = ma$, which is to become known as Newton's Second Law.[38] It is this relationship in concert with Newton's Law of Universal Gravitation that is to supply the method of analysis for centuries to come. Kepler used Tycho Brahe's astronomical data to arrive at two of his empirical laws of planetary motion in his *New Astronomy*. Newton used his Second Law of Motion ($f = ma$) and his presumption of a Universal Law of Gravitation to derive the explicit mathematical nature of the gravitational force.

The second step in the solution is to expand the scope of the problem to include the effect of other bodies: i.e., the simultaneous effect of the sun and other planets on the motion of the planet in question. It is an attempt to make the initial ideal problem (a single planet about a single force center) conform more closely to the actual problem. The solution by Newton in the *Principia* does not directly apply gravitational theory and the new calculus in the exact form employed by the Newtonians to follow. Nevertheless, Newton's solution provides the model.

In the third and final step, the result must be compared to the actual values of observation and, given theoretical and experimental limitations, it must be judged in light of the match between the predicted and observed values. In insisting on such a careful match between astronomical predictions and observations, Newton carries on a long established tradition.

The Extended Disciplinary Matrix

I. *Symbolic generalizations:* But Kuhn argues that such concrete problem-solutions reveal more than just how-to-do-it. Careful inspection of the set of exemplars reveals evidence of other elements of the disciplinary

matrix. The particular application of the gravitational force represents a special case of the "f" in Newton's second law, f = ma, and the mass of the planet is the "m" in the law. The acceleration is represented by "a" and mathematical methods exist for getting from it to knowledge of the path of "m" in space and time. This law is an example, Kuhn tells us, of the element of the disciplinary matrix that he calls a "symbolic generalization." These generalizations look like laws of nature but they serve a wider function. Kuhn claims that "they function in part as laws but also in part as definitions of some of the symbols they employ."[39] It is this second function that undergoes a change in a "revolution" and thus permits the formal expression of the law to remain unchanged.

II. *Metaphysical parts:* One should also find traces of commitment to the element of the disciplinary matrix called the "metaphysical parts"; i.e., to belief in items that have to do with the essential nature of reality and as such are beyond direct physical demonstration. Kuhn gives as an example the belief in matter and force.[40] Immediately upon the publication of the *Principia*, and for some time following, there was considerable controversy over the existence of such an "occult" thing as a gravitational force that mysteriously reached out over enormous celestial distances to act on bodies. But as early as the second edition of the *Principia* in 1713, the editor of the preface placed such objections outside the realm of science. He stated, "Therefore gravity can by no means be called an occult cause of the celestial motions, because it is plain from the phenomena that such a power does really exist."[41] What is plain, however, is that if one believes that force exists and if one learns to use force the way Newton used it in the *Principia*, then one can solve problems that one's colleagues will agree are important. So good Newtonian astronomers must not waste time arguing about such questions as the existence of forces in general, or of gravitational forces

in particular, for it is *obvious* from the tremendous success of the *Principia* that force does exist. To this belief in the existence of gravitational force, one can also add a belief in its universality. It has the same nature on the moon and on Mars as it has on earth, even though no one had ever been to the moon or to Mars. Newtonian astronomers also believe that planets move about the sun and not about the earth. The belief is so universal, however, that Newton did not even raise this once controversial question in the *Principia*. All Newtonian astronomers *know* that the sun is fixed, even though the relative motion of Mars to earth would be the same if the earth were stationary and the sun moved with Mars revolving about it.

III. *Shared values:* Finally, the nature of the solution to the problem of Mars given in the set of exemplars in the *Principia* should reveal traces of the element of the disciplinary matrix that Kuhn calls "shared values." As an example, he suggests that "probably the most deeply held values concern predictions: they should be accurate; [and] quantitative predictions are preferable to qualitative ones."[42] Book III of the *Principia* demonstrates clearly that Newtonian astronomy is devoted to fitting experimental evidence to the quantitative theoretical predictions of Books I and II.

B. Greek Geometrical Astronomy

The Kuhnian disciplinary matrix called Ptolemaic astronomy is to be defined by the activities of the enduring group of adherents attracted to astronomy by the Greek astronomer Ptolemy, in his *Almagest*, and its Kuhnian set of exemplars are to be found in the problems, answers, and demonstrations contained within this work.[43] The *Almagest*, like the *Principia*, is particularly well-suited to supplying exemplars. After the first few descriptive pages of Book I, it continues on for another 400 or 500 pages of demonstrations, problems, and solutions. As Newton's
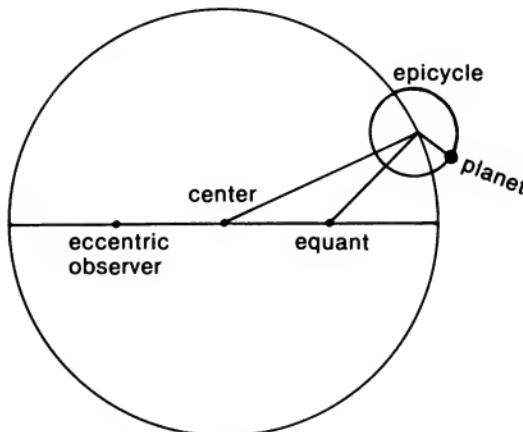
FIG. 1. The basic Ptolemaic scheme for the motion of a planet such as Mars. None of the devices are drawn to scale.

Principia served astronomy through the eighteenth and nineteenth centuries, so Ptolemy's *Almagest* served astronomers from the second century A.D. until the seventeenth century. Kepler, in fact, comments that Copernicus would have been well advised to spend less time looking at Ptolemy and more time looking at the heavens.

To parallel the discussion of Newtonian astronomy, one should here present the sample solution from the Ptolemaic set of exemplars and then identify in it the other elements of the disciplinary matrix suggested by Kuhn. The reason that this approach worked so well for the *Principia* (assuming that it did) was that we live in a Newtonian world and are already familiar with elements such as a belief in mass and force that surface naturally from the example (after all, it is *obvious* that mass and force exist). What must be done with Ptolemaic astronomy is just the reverse: first identify the metaphysical principles that were obvious for both Ptolemy and all western astronomers from the fourth century B.C. until the sixteenth century A.D.; and second, inspect the set of exemplars to discern the influence of these principles.

There are three clearly discernible metaphysical principles in Greek astronomy.

Metaphysical Principles

The first metaphysical principle is the belief in GEOCENTRICITY: the earth is stationary and it is in the center of the universe. This view has a great appeal to "common sense," although a moving earth did occur in the Pythagorian celestial scheme. Ptolemy discusses this question in Book I and argues that everything points to a static central earth.

The second metaphysical principle is the belief in CELESTIAL CIRCULARITY: celestial bodies move in combinations of perfect circles. It may not have the same current common sense appeal as geocentricity but its source is one of great authority: Plato. In Plato's *Timaeus*, the world is described in terms of form and copy. Form having been previously defined in the *Republic*, it is clear in what sense the physical world is a copy. A particularly interesting question thus arises concerning the nature of time. Forms of course are eternal, unchanging, and timeless. What

then is the copy of eternity in this world of change? Plato tells us that "Time is the moving image of eternity." The movement that mirrors eternity must reflect the endlessness and uniformity of eternity. Such endless motion exists only in the circularity of celestial motion. There is no beginning or end to the circle just as there is no beginning or end of celestial motion. The fixed stars clearly move in endless and uniform circles and they are the celestial clocks that are the copy of the eternity of the forms. Is this Platonic defense of celestial circularity stronger than that of the Newtonian defense of the existence of force? The answer to such a question is irrelevant. The essential point is that it was everywhere the common consensus among astronomers. It is obvious that celestial motion must be circular. That the planets appear to move in a more complicated fashion does not disturb this conviction of circularity. Rather, Plato sets the challenge to seek out the set of circular motions, which will, when properly combined, "save the phenomena." In Kuhn's terms, Ptolemaic astronomy was "sufficiently open-ended to leave all sorts of problems for its practitioners to resolve."

The third and final metaphysical principle is the belief in the LUNAR DICHOTOMY: the clear physical separation between the unchanging heavens above the lunar sphere and the changing world below. It also has a very authoritative source: Aristotle. He agrees with Plato on the existence of forms, except that Aristotle would not have them exist beyond the world but rather would have them made manifest in matter. Aristotle separates the universe into two distinct parts: that which lies above the lunar sphere (*i.e.*, the sphere generated by the radius of the moon's motion about the earth), and that which lies below the lunar sphere. Here below, one finds the basic elements of air, earth, fire, and water, which can change one into the other. Here is generation and corruption: *i.e.*, things come into being and they pass away. Above the lunar sphere, however, exists a fifth element called "aether" that is perfect and unchangeable. On the one hand, comets must lie below the lunar sphere, for they come into being and pass away. On the other hand, planets and stars must lie above it because they are indestructible. This lunar dichotomy was a common consensus of Ptolemaic astronomers.

Set of Exemplars

It remains, therefore, to see how the set of exemplars in the *Almagest* reveals the implicit acceptance of these three metaphysical principles. The nature of the solution to the problem of the motion of Mars is indicated in figure 1, which is from a modern text but is faithful to the *Almagest*. The planet itself moves uniformly around a small circle called an epicycle. The center of the epicycle in turn moves about a larger circle called a deferent. Note, however, that the earth is not at the center of the larger circle, but is eccentric to it. This eccentric position of the earth is not a violation of geocentricity because it can be shown that the eccentricity can be replaced by adding yet another epicycle with the earth at the actual center. Thus the eccentric earth is only a convenience, not a necessity. The critical item to notice, however, is the *equant* point. This device is Ptolemy's unique contribution to the analytical devices of Greek astronomy. What it does is to separate the motion of the center of the epicycle into two distinct parts: one of circularity and one of uniformity. In Kuhn's terms, this is an "*ad hoc* adjustment of a prevalent epistemological theory" to eliminate the apparent conflict between the observed motion of Mars and the predicted results that are possible with existing devices: i.e., epicycles without equants. To make the data fit, Ptolemy needs the equant. The equant violates the pure rule of combined uniform circular motion of Plato. Thus the rule must be modified to the extent that the

circularity and uniformity are at least separated (but not discarded).

These Ptolemaic devices are capable of treating the very elliptical motion of Mercury as well as the more circular motion of Mars. For Mercury, the center of the deferent itself moves in a circle about a point that is neither the equant point, nor the earth. The net result is that the effective deferent is an oval. In fact, Mercury is difficult to observe because of its constant proximity to the sun. Thus the Ptolemaic oval is in no way an empirical forerunner of the Keplerian ellipse. Nevertheless, it does display the versatility of the Ptolemaic model. To any earlier astronomer who may have been tempted to blame the metaphysical presumption of circularity for his failure to handle such problems, Ptolemy might have correctly admonished him by saying, "It's a poor carpenter who blames his tools."

Other Elements of the Disciplinary Matrix

What then of the other elements of the disciplinary matrix that Kuhn has identified? It is of interest to find in Ptolemaic astronomy a symbolic generalization comparable to Newton's second law, f = ma. For Ptolemaic astronomy, the symbolic generalizations are the circular and uniform elements of epicycles, eccentrics, and equants that provide the basic tools of analysis for astronomers from the second to the seventeenth century. They express simultaneously the law of celestial motion and the definition of what it is, i.e., circular, in the same way that f = ma expresses a law and a definition.

As for the last element, shared values, one need only restate the value on predictions given for Newtonian astronomy. The *Almagest* is as concerned with theoretical quantitative predictions and their fit to observational data as is the *Principia*. For Ptolemy, the experimental error is typically 10 minutes of arc or more, while for Newton,

it is typically 2 minutes of arc or less, but both share the same concern for the fit of theory and observation. That both of the disciplinary matrices have a common shared element is not in violation of Kuhn's view of science. In fact, he suggests that values of this sort often survive the revolutions.[44]

C. The Kuhnian Astronomical Revolution

Thus far the discussion has been concerned with the Newtonian disciplinary matrix that was established in the eighteenth century and the Ptolemaic disciplinary matrix that remained unchallenged until the middle of the sixteenth century. It remains, therefore, to look at this century and a half of transition that justly deserves the title of "revolution." In *The Structure of Scientific Revolutions*, Kuhn describes the characteristics that such revolutions must share. The sense of Kuhn's scientific revolution is close to what is commonly understood by a political revolution, and Kuhn uses this analogy: "Like the choice between competing political institutions, that between competing paradigms proves to be a choice between incompatible modes of community life."[45] Thus the Kuhnian scientific revolution calls for a switch in paradigms, used in the universal sense of disciplinary matrices, just as political revolutions call for a switch in political institutions. Moreover, Kuhn sets out the two essential characteristics of a classic work that is to serve as a paradigm in the limited sense of sets of exemplars.

Their achievement was sufficiently unprecedented to attract an enduring group of adherents away from competing modes of scientific activity. Simultaneously, it was sufficiently open-minded to leave all sorts of problems for the redefined group of practitioners to resolve. . . . Achievements that share these two characteristics, I shall henceforth refer to as a 'paradigm'.[46]

Without these two 'bandwagon' characteristics there can be no new paradigm, and hence no Kuhnian revolution.

Thus Copernicus's *Concerning the Revolutions of the Celestial Spheres* cannot serve, in Kuhn's terms, as the central set of exemplars in a new disciplinary matrix, i.e., no paradigm switch or 'revolution' has taken place. Quite clearly there has been a dramatic personal conversion for Copernicus, but a revolution requires community participation. The Kuhnian test for identifying a central element in a new disciplinary matrix requires that it share the two essential characteristics of the 'bandwagon effect,' and here it falls short. One can name a number of astronomers in Germany, England, and Italy who supported Copernicus's work. But it never had the following that was enjoyed by the *Almagest* before it nor the *Principia* after it.

One is also faced with the problem that arose even in the anonymous preface of *Concerning the Revolutions of the Celestial Spheres;* i.e., is the motion of the earth merely a mathematical convenience or does it represent a physical fact? The basis of the argument was laid in antiquity in the Platonic charge of "saving the appearances" and continued to be a vital question through the trial of Galileo in the early seventeenth century. Thus even those who praised the work and used it, may have done so with major reservations concerning the basic premise of a fixed sun and a moving earth. The historian J. L. E. Dreyer discusses the reception given it by the German astronomer Erasmus Reinhold, who had hailed Copernicus's work as opening a new era and who had prepared new tables of celestial motion, the Prutenic Tables, based on the analysis and constants of *Concerning the Revolutions of the Celestial Spheres.* Because of the lack of new and dependable observations, the tables were not a great improvement over the Alfonsine Tables that they replaced. Nevertheless, they represented a step forward. But, Dreyer claims, all of this could have been done without a fundamental conversion: "There was no occasion for Reinhold to make a confession of scientific faith, and he gave no

hint to whether the system of Copernicus was the physically true one or not."[47]

Elsewhere in Germany, there were other astronomers who supported Copernicus. Most notable was Michael Maestlin of Tübingen University, who was to be the mentor of the great Kepler. But it was not widely adopted by sixteenth-century astronomers and despite its fundamental re-orientation of the basic framework of mathematical astronomical calculations, it does not qualify, in a Kuhnian sense as a paradigm shift, i.e., as an astronomical revolution. Neugebauer attributes whatever revolutionary flavor the work has to modern hindsight and maintains that as it stood, it simply perpetuated the Ptolemaic system.

Modern historians, making ample use of the advantage of hindsight, stress the revolutionary significance of the heliocentric system and the simplifications it had introduced. In fact, the actual computation of planetary position was exactly the ancient pattern and the results are the same. The Copernican solar theory is definitely a step in the wrong direction for the actual computation as well as for the underlying cinematic concepts. The cinematically elegant idea of secondary epicycles for the lunar theory and as a substitute for the equant . . . does not contribute to make the planetary phenomena easier to visualize. Had it not been for Tycho Brahe and Kepler, the Copernican system would have contributed to the perpetuation of the Ptolemaic system in a slightly more complicated form but more pleasing to philosophical minds.[48]

But revolutions, scientific, political, or Kuhnian, are never represented by a single work or event. Rather, they take place over an extended period of time. The historian Crane Brinton offers a model for political revolution in his book *Anatomy of Revolution.* He identifies four stages that are of importance. The first he calls the "Old Regime," which is a period of increasing unrest. The second he calls the "Honeymoon Stage" and it is the rule of the moderates or the calm before the storm. The third stage is the

"Accession of the Extremists" and here Brinton discusses the reign of terror and the reshaping of society. The fourth and final stage he calls "Thermidor" or the calm and euphoria after the storm. This model works well for Brinton for the French Revolution but less well for the others, i.e., the American, the Russian, and the British industrial revolution. Nevertheless, it will serve, however imperfectly, to delineate the steps of the astronomical revolution viewed from the vantage point of Kuhn's structure. Kuhn himself is fully aware of the extended nature of revolutions. In the concluding chapters of his earlier work, *The Copernican Revolution*, he discusses a larger revolution in science and cosmology that he calls the Newtonian revolution. This larger revolution is one "which began with Copernicus and through which the Copernican Revolution was at last completed."[49] Thus for Kuhn the Newtonian revolution extends beyond the limits of an astronomical revolution and results in the eighteenth century's vision of a "Newtonian world machine." The more limited astronomical revolution has, for Kuhn, an earlier terminus. "In so far as the Copernican Revolution was a revolution in astronomical thought, its story ends here [the close of the seventeenth century]."[50]

Thus the astronomical revolution that provides the transition from the Aristotelian world view, as reflected in the *Almagest*, to the Newtonian world view, as reflected in the *Principia*, takes place over an extended period of nearly one hundred and fifty years. I have selected three published classic works that can serve as guides through this period. They cannot serve individually as the central element of a disciplinary matrix in the same sense as the *Almagest* and the *Principia*, for there are no "enduring group of adherents" for whom they serve as a source of a set of exemplars. They can, however, be identified in Brinton's terms with various stages of the revolution. Moreover, it is possible to identify with each work a change of one of the three

metaphysical parts identified in the previous discussion of Ptolemaic astronomy. Clearly the development of astronomy in this critical period of intellectual flux is much more complicated than such a simplified analysis implies. But hopefully it serves to make clear in broad strokes what is implied in Kuhn's description of scientific progress.

All historians of science would consider the following three works as critical: (1) Copernicus's *Concerning the Revolutions of the Celestial Spheres*, published in 1543, (2) Kepler's *The New Astronomy*, an analysis of the motion of Mars, published in 1609, (3) and Galileo's *The Starry Messenger*, a report of his telescopic observations, published in 1610. Each of these works is a classic in itself, as fully deserving of that title as the *Almagest* and the *Principia*. Each plays a vital role in the revolution, but it is not until the *Principia* has been accepted as the central set of exemplars that the revolution is complete. I shall argue in Brinton's terms that Copernicus plays the role of the moderates in responding to the unrest surrounding the "Old Regime" of the *Almagest*, that Kepler, Galileo, and Newton represent the "Accession of Extremists" who reshape the society, and that the eighteenth century is the "Thermidor," the calm and euphoria after the storm. In Kuhn's terms it is possible in a simplified fashion to identify an anomaly in the sense of an unsolved puzzle that served as a focus of interest for each of these works: the "anomaly" that represents Copernicus is theoretical in origin, the "anomaly" that represents Kepler is experimental in origin, and the "anomaly" that represents Galileo is instrumental in origin.

Copernicus and "Geocentricity"

Two important central chapters of *SSR* are entitled "Anomaly and the Emergence of Scientific Discoveries" and "Crisis and the Emergence of Scientific Theories." In each Kuhn gives three examples: the discoveries

of oxygen, x-rays, and the Leyden jar are solutions to the puzzles that were the anomalies; the theories of Copernican astronomy, eighteenth-century chemistry, and Maxwell's electromagnetism are the response to the crisis faced by astronomy, chemistry, and physics in the fifteenth, eighteenth, and nineteenth centuries respectively. Clearly the more limited anomaly is related to the larger crisis and Kuhn anticipates an overlap: "The sorts of discoveries considered in the last section (anomalies) were not, at least singly, responsible for such paradigm shifts as the Copernican, Newtonian, chemical, and Einsteinian revolutions."[51] It is important here to understand that by the "Copernican revolution" Kuhn means the astronomical revolution that begins with Copernicus and ends with Newton. By the "Newtonian revolution" Kuhn means the larger revolution in science and cosmology that also begins with Copernicus but that goes well beyond astronomy in its scope [see note 49]. Copernicus's *Concerning the Revolutions of the Celestial Spheres* provides a first critical step in the revolution, but neither it nor Newton's *Principia* is to be thought of singly as being responsible for a revolution.

Nevertheless, the role of Copernicus in the revolution is by far the most challenging. It is relatively easy to understand the motivation for a final work such as the *Principia* or of an intermediate work such as *The New Astronomy*; but what is the "crisis" in astronomy that motivates Copernicus to take this revolutionary initial step? Kuhn points out in *SSR* that "Copernicus himself wrote in the Preface to the *De Revolutionibus* that the astronomical tradition he inherited had finally created only a monster."[52] In his earlier work on Copernicus, Kuhn states that "diffuseness and continued inaccuracy—these are the two principle characteristics of the monster described by Copernicus."[53]

In *SSR* Kuhn takes up again the issue of "continued inaccuracy." He claims that "the state of Ptolemaic astronomy was a scandal before Copernicus' announcement."[54] He documents this statement with a reference to a work by A. R. Hall that contains a similar charge. "Unfortunately it was well known by 1500—it was a scandal to learning—that calculations were not verified by observation."[55] Hall concludes that Copernican tables were much better than the Alphonsine tables and that "the improvement can be attributed to the greater accuracy of the Copernican calculations."[56]

But the astronomer and historian Owen Gingerich challenges this claim. He has used modern planetary theory and computers to calculate where planets were in the sixteenth century. Moreover, he has compared the calculations of a sixteenth century Ptolemaic astronomer (Stoeffler, died 1530) with the calculations of a sixteenth century Copernican astronomer (Stadius, born 1527). Gingerich states that "the first result of this comparison is the fact that the errors reach approximately the same magnitude before and after Copernicus."[57] Thus if the state of predictive astronomy was "a scandal before Copernicus' announcement", then clearly it remained so immediately after that announcement. Kuhn recognizes that situation, for in *SSR* he states "unlike Kepler, the Copernican theory scarcely improved upon the predictions of planetary positions made by Ptolemy."[58]

The second face of Copernicus' monster, as viewed by Kuhn, is "diffuseness." If this statement is taken to mean that the Copernican system is *simpler* than the Ptolemaic, then it is clearly wrong. Neugebauer, Gingerich, and others have clearly pointed out that this "myth of simplicity" has no foundation in fact. In terms of the detailed calculations for any particular planet, Gingerich claims that it "would have been very difficult for Copernicus' contemporaries to distinguish between the two schemes on the basis of complexity."[59] But Kuhn's reference to "diffuseness" rises above mere simplicity. He is concerned with the many Islamic and Eu-

ropean astronomers who had generated 'modified Ptolemaic' systems. "There were so many variant systems, the adjective "Ptolemaic" had lost much of its meaning. The astronomical tradition had become diffuse."[60] And in *SSR*, Kuhn claims that the monster revealed in the preface to *De Revolutionibus* "provides one of the classic descriptions of a crisis state."[61]

Gingerich suggests, however, an alternate view of what motivates Copernicus. He points out that in the preface Copernicus faults other systems for failing to discern in the design of the universe a "fixed symmetry of its parts" and thus creating a "monster rather than a man."[62]

This "fixed symmetry of its parts" refers to the fact that, unlike in the Ptolemaic scheme, the relative sizes of the planetary orbits in the Copernican system are fixed with respect to each other and can no longer be independently scaled in size. . . . Clearly, this interlinking makes the unified man, and in contrast the individual pieces of Ptolemy's arrangement become a monster.[63]

Thus from Gingerich's point of view the challenge faced by Copernicus arises in the initial formulation of the Ptolemaic system with its separate parts rather than with the various revisions of the system itself as suggested by Kuhn. Therefore, if this challenge represented a crisis, Gingerich claims, it is one that should have been in force from the time of Ptolemy himself and its role as crisis for Copernicus is thus severely limited.

It is not the charge of this paper, however, to evaluate how well Kuhn's model fits astronomical history, but rather to use the latter to describe the former. The historian Koyré provides an alternative source of crisis that serves this function. He suggests yet another and more specific motivation for Copernicus' innovation can be found in his earlier work the *Commentariolus*. "It [the *Commentariolus*] reveals far better than the latter work [*De Revolutionibus*] some of the considerations that guided the mind of Coper-

nicus."[64] The preface to the *Commentariolus* is quite short, three paragraphs, and the final paragraph clearly sets out Copernicus' concern.

The theories concerning these matters that have been put forth far and wide by Ptolemy and most others, although they correspond numerically [with the apparent motions], also seemed quite doubtful, for these theories were inadequate unless they also envisioned certain *equant* circles, on account of which it appeared that the planet never moves with uniform velocity either in its *deferent* sphere or with respect to its proper center. Therefore a theory of this kind seemed neither perfect enough nor sufficiently in accordance with reason.[65]

Seen in this fashion, the equant violates the Platonic charge to employ uniform circularity to explain celestial motion because the equant separates uniformity from circularity. The attempt to eliminate the equant is thus an attempt to return to first principles. The price that must be paid to restore the metaphysical principle of celestial circularity to its pristine form is the destruction of the metaphysical principle of geocentricity. Although Kuhn does not dwell on the equant as motivation, he clearly recognizes the general results: "In Copernicus' work the revolutionary conception of the earth's motion is initially an anomalous by-product of a proficient and devoted astronomer's attempt to reform the techniques employed in computing planetary position."[66]

Thus Copernicus is to be seen as a devoted Aristotelian who would restore to celestial motion the Platonic uniformity that Ptolemy's equant had tarnished. The cost was the shift of the center of Plato's celestial circularity from the Earth to the Sun. Thus the metaphysical principle identified as geocentricity, which assumed a stationary Earth, has been replaced by the assumption that it is the Sun that is stationary and the Earth that moves. Celestial bodies still do not require Newtonian "occult forces" to move them in their natural circles, and the celestial perfec-

tion of the heavens remains unchallenged. Copernicus challenges the metaphysical principle of geocentricity but he holds to the principles of celestial circularity and the lunar dichotomy. Therefore, as Kuhn claims, *Concerning the Revolutions of the Celestial Spheres* is "a revolution-making rather than a revolutionary text."[67]

Kepler and "Celestial Circularity"

As one places Copernicus on a level with Ptolemy, so one must also place Kepler on a level with Newton, both with regard to the intensity and creativity of their work and with its ultimate value to astronomy. Kepler sought throughout his life to understand the order that God had imposed on the universe. He looked for archetypal cause, expressed in geometry, music, and astronomy, that would reveal the Creator's master plan. He inherited from Tycho Brahe not only astronomical data but the conviction that there were no crystalline spheres to carry around the planets. Thus he also looked for physical cause in astronomy, but as an extension and manifestation of archetypal cause, not as a substitute for it. He sought to know why there were only five planets and why they were spaced as they were. He sought to know the precise path of the planets and their exact positions on that path. Finally, he sought to bring it all together in a great expression of God's "world harmony."

By the end of the sixteenth century, the great observational astronomer Tycho Brahe had completed his new and precise measurements of planetary motion. Fortunately, upon his death these new measurements were in the hands of Johannes Kepler, mathematician and astronomer without peer. The improved measurements of the motion of Mars were the source of a new "anomaly" whose solution proved so evasive and produced such a "crisis" that Kepler was driven to bend the rules even further. It is interesting to watch the initial conflict between Kepler's

allegiance to celestial circularity (Kuhn's metaphysical parts) and his devotion to accuracy (Kuhn's shared values). Tycho's data for Mars was at least an order of magnitude more accurate than either Ptolemy's or Copernicus's data. No matter how the celestial circles were manipulated by Kepler, the differences between the calculated positions and measured positions could not be reconciled. The motion of Mars remained an anomaly. The puzzle could not be solved. Finally, in desperation, Kepler set aside the circles and began to experiment with other geometrical shapes to describe planetary motion. He bent the rules. He abandoned the Platonic charge. The final solution was not a combination of uniform circular motions, but an ellipse along which the planet moved with an orderly but varying speed. The metaphysical principle of celestial circularity was under attack. In *The New Astronomy*, he recorded in great detail all of his mistakes and false trials as well as his final success. These details were a source of difficulty for the aspiring seventeenth-century astronomer who wanted to get the point, but a gold mine for the historian or philosopher who is concerned with how the progress was achieved. Arthur Koestler, in his book *The Sleepwalkers*, discusses Kepler's repeated failure to recognize the orbit of Mars as an ellipse, when (from hindsight) it should have been *obvious* to anyone with Kepler's training that it must be an ellipse. But metaphysical convictions die slowly. When the realization did dawn on Kepler, he expressed his reaction by saying, "I felt as if I had been awakened from a sleep."[68]

But even with Kepler the revolution had not yet taken place. There was no "enduring group of adherents that was attracted away from competing modes of scientific activity." Galileo knew of Kepler's work but clearly he had not read it. Seventy years later, even Newton had some initial doubts about the exactness of Kepler's results.

So Kepler's *New Astronomy*, however

powerful, must be relegated to the role of an "*ad hoc* modification" of theory. And a closer examination of Kepler's other work does not counter that suggestion. Planetary circles may have been destroyed but God the Creator was still God the Geometer and He and His world spoke to Kepler in the language of geometry. Although questions of physical causes (such as the forces of Newton) are important in Kepler's work, the geometric causes still dominated. He maintained a continued interest in astrology, and ten years after *The New Astronomy*, he published *The Harmony of the World*, a work in which the heavens abound in a harmony expressed in planetary positions and motions that can be recited and revealed in the circular harmonies of music. It was here that Kepler found a deeper sense of celestial circularity and, moreover, was convinced that the elliptic orbit did not destroy celestial circularity but was in fact necessary to preserve it.[69] That conviction, however, died with Kepler, and the elliptical orbits of the *New Astronomy* eventually were responsible for the overthrow of the Ptolemaic metaphysical commitment to celestial circularity.

Galileo and "Lunar Dichotomy"

The removal of the "Lunar Dichotomy" was the final step in the revision of the metaphysical principles of astronomy necessary for the coming of Newtonian astronomy, and it was provided by Galileo and his telescope. It clearly is an oversimplification to credit this step only to Galileo. It is foreshadowed when Copernicus sets the earth in motion and it is dramatically advanced when Kepler introduces celestial physical causes, such as magnetic effects, that have terrestrial counterparts. Nevertheless, this revision achieves its fruition in the work of Galileo. The work of interest is not his great polemical defense of the Copernican system, the *Dialogue Concerning the Two Chief World Systems* of 1632. That work is more an attack

on the Scholastic Establishment than a work of science and as such does not fit into the analysis of astronomy. What little astronomy it does contain is ignorant of the work of Kepler. Rather, of interest is Galileo's small work of 1610, entitled *The Starry Messenger*, in which he reports the details of his observations of the heavens with his telescope. The "crisis" is induced by the appearance of the new instrument and the information it reveals. It is not, however, improved accuracy or more details of planetary motion that he reports. Rather, he publishes his observations of the things he has seen on the surface of the moon. Now the last of the three metaphysical elements of Ptolemaic astronomy has fallen. The moon is not an Aristotelian example of celestial perfection. Rather, it has a surface that contains mountains and craters such as may be found on the earth. The distinction between the nature of terrestrial and celestial worlds is gone. The lunar dichotomy is abolished.

"Comes the Revolution"

Thus the road is clear for the coming of a "universal" gravitational force that causes objects to fall to the earth, that causes the moon to move about the earth, and that causes the earth to move about the sun. It will require the great genius of Newton to breathe life into the system with his *Principia*, but *Concerning the Revolutions of the Celestial Spheres, The New Astronomy*, and the *The Starry Messenger* have cleared the path. There can be no revolution from an existing paradigm without a simultaneous switch to a new paradigm. There is no paradigm without an "enduring group of adherents" and an "open set of problems" for them to work on. The "set of exemplars" that is the *Principia* could not have been conceived and would not have been received if the adjustments had not been made in the constellations of shared beliefs, metaphysical principles, and symbolic generalizations that surrounded it.

These adjustments, "*ad hoc* or not", were the work of the genius of Copernicus, Kepler, and Galileo. But it was Newton and the *Principia* that gave rise to the enormous flood of scientific activity and identification that was science in the eighteenth and nineteenth centuries. It was in 1687 that the central set of exemplars necessary for a successful Kuhnian revolution finally appeared.

Conclusion

Thus the "Copernican Revolution," of which Kuhn wrote in 1957, when analyzed in terms of the structure of scientific revolutions, of which Kuhn wrote in 1962 (*SSR*), occurs not with Copernicus, in 1543, but with Newton in 1687![70] This conclusion is not so paradoxical as it first appears. Kuhn's early work on Copernicus is an exercise in the history of science, as is his later work on the "Quantum Revolution."[71] In neither work, one written before and one written after his *SSR*, does Kuhn attempt to analyze the particular historical period in terms of the structure of science that he details in *SSR*.[72] There are distributed references in *SSR* to Copernican and Newtonian concepts, but there is no attempt at presenting them as a single, unified, case study. This attempt was undertaken in this paper fundamentally to explain Kuhn's analysis of the structure of science, rather than to defend or to attack it. Nevertheless, there emerges a strong correspondence between the major elements in the history of astronomy and those in Kuhn's view of the structure of science. Perhaps such a correspondence would break down under a closer detailed inspection. Moreover, the extension of this correspondence to other areas of science may not be as strong. The work of Stegmüller in classical mechanics, however, indicates that it is useful in the area of mathematical physics (see notes 17 and 18). On the other hand, Kuhn's conclusions concerning the nature of scientific knowledge and progress do not find universal approval. Many critics claim that he presents a view of science that is relativistic and irrational.[73] But even if he has succeeded only in providing philosophers of science with a useful model of a limited portion of scientific activity, the major elements of mathematical astronomy, then Kuhn has produced a work worthy of the attention it has received.

Acknowledgments

Notes

1. Kuhn, 1962. A slightly revised second edition with a postscript was published in 1970. All references will be to that second edition.
2. Coughlin, 1982: 21–23.
3. See the Appendix for a listing of these reviews.
4. Gutting, 1980: 321–339. See the bibliography for an extensive listing of works by and about Kuhn.
5. Kuhn, 1977: xix.
6. Kuhn 1977: 294.
7. Lakatos and Musgrave, 1970: 383–394.

8. Lakatos, 1970: 383.
9. Lakatos, 1970: 61–65.
10. Kuhn, 1970: 174.
11. Kuhn, 1970: 181.
12. Kuhn, 1970: 182.
13. Kuhn, 1977: xviii–xix. It is important to note that Kuhn here refers to sets of standard examples, such as appear at the end of chapters in textbooks of physics, and not simply to a single solution of historic importance that in some way acts as a source for all similar solutions to follow, i.e., the Newtonian solution of the Keplerian problem of elliptical planetary orbits. Such an outstanding problem/solution example clearly is part of the set of exemplars found in any physics textbook. Newton himself was aware of its importance when he referred in the *Principia* to "the dignity of the problem." The modern version of the Newtonian solution to the Keplerian problem will appear as the central example within the chapter dealing with motion under central forces and variations of it will appear in the problem sets at the end of the chapter. But Kuhn's reference is to the entire set, both the central example and its more mundane textbook images. And it is within this larger set that the essential importance of exemplars lies.
14. Kuhn 1977: 305.
15. Kuhn 1977: xix and 229.
16. Kuhn 1977: xx.
17. Stegmüller, 1976: 178.
18. "Stegmüller, approaching my work through Sneed's has understood it better than any other philosopher who has made more than passing reference to it." (Kuhn, 1976: 179.)
19. Williams, 1980: 68.
20. Lugg, 1979: 289.
21. On a few occasions, Kuhn will refer to a matrix element other than the central one representing the set of exemplars as a paradigm. It will always be an outstanding attribute by which an entire community can be identified but strictly speaking it is not a paradigm in either of the two senses that he has identified in the postscript. For example, "To be accepted as a paradigm, a theory must seem better than its competitors." [Kuhn, 1970: p. 184.] A theory such as the "Kinetic Theory of Gases" is included in the matrix element that Kuhn calls "metaphysical committment." [Kuhn, 1970: p. 184.] To refer to it as a paradigm is not consistent with the two redefinitions of that term. But that theory is the most visible single attribute of the group identified as "kinetic theorists" and Kuhn uses it very loosely to stand for the entire disciplinary matrix and hence the global sense of paradigm.
22. Kuhn, 1970: 182–184.
23. Kuhn, 1970: 184.
24. Kuhn, 1970: 184–186.
25. Kuhn, 1970: 43.
26. Kuhn, 1970: 40.
27. Kuhn, 1970: 41.
28. Kuhn, 1970: 41.
29. Kuhn, 1970: 40.
30. Kuhn, 1977: 35–36.
31. Kuhn, 1970: 52. An example of such an anomaly is the inability of 19th-century physics to solve the problem of "black-body radiation". Moreover, the solution that resulted from careful application of classical physics to this problem (the so-called "violet catastrophe") made no sense. Nevertheless, the expectation of contemporary physicists was that eventually classical physics would solve this enigma.
32. Kuhn, 1970: 77.
33. Kuhn, 1970: 78.
34. Kuhn, 1970: 77.
35. Kuhn, 1970: 78. In terms of the example of black-body radiation given in footnote 31, the solution given by Planck required the "quantum postulate" to correctly steer between the Charybdis and Scylla that were the classical solutions of Wien and Rayleigh. It is only in retrospect that the persistent failure of classical physics to solve this puzzle is seen to argue for a flaw in classical physics. The anomaly is not perceived as a counterinstance even when Rayleigh produces an "exact" classical solution that is classically impossible. It is only after the discipline is driven to accept the drastic change of the quantum postulate that the puzzle of black-body radiation (now solved) appears as a counterinstance relative to classical physics.
36. Kuhn, 1970: 10.
37. Kuhn, 1970: 10.
38. The first analysis in the form of f = ma, which was to become the hallmark of Newtonian astronomy, was published in the middle of the eighteenth century by the German physicist and mathematician, Euler. In the *Principia*, Newton gave this Second Law of Motion as "The change of motion is proportional to the motive force impressed; and is in the direction of the right line in which that force is impressed." Its employment in the specific problem solutions is not as direct as in Euler's solutions and in those to follow. Newton employs a mixture of geometry and limiting processes (clearly suggestive of the techniques of calculus) to develop a relationship that could be called the "Geometric Key." It is this mixture that unlocks the solutions for Newton and that in turn provides the prototype for Euler's revision.
39. Kuhn, 1970: 183.
40. Kuhn, 1970: 184.
41. From Roger Cote's preface to the second edition of the *Principia*. (Newton, 1971: xxvii.) The Latin original of this English translation was published in 1713, some 25 years after the first Latin edition of 1687.
42. Kuhn, 1970: 185.
43. Ptolemy, 1954: 1–495.
44. Kuhn's descriptions of the extent of change involved in a scientific revolution ("when paradigms change, the world itself changes with them") often leaves one at a loss to identify an element that would survive. For Kuhn, however, the element of the disciplinary matrix that he has called "shared values" does persist. In particular, the astronomer's concern for theoretical quantitative predictions and their ability to fit to observational data appears to be uni-

versal. There have been great strides taken within the last fifty years to understand details of Babylonian mathematical astronomy. Otto Neugebauer and his colleagues have provided translations of cuneiform astronomical and astrological tablets. Moreover, they have been able to understand the mathematical methods employed in making the theoretical predictions. (Neugebauer, 1975; 3 vols.) In a short but informative paper, A. Aaboe, a colleague of Neugebauer, sketches the character and content of Babylonian scientific astronomy. (Aaboe, 1974: 21–42.) The set of exemplars displayed by the cuneiform astronomical tablets is distinctly arithmetical in contrast to the geometrical methods of the *Almagest*. Moreover, these tablets do not display an interest in the continuous path of the planets, as do the *Almagest* and the *Principia*. Rather they are primarily concerned with the location of the planets at five specific points: first and last visibility, the two stationary points (retrograde), and opposition. Despite these fundamental and pronounced differences from Greek astronomy, the theoretical calculations are detailed and precise, and they are carefully compared to the points observed. This concern for accurate predictions reveals a common bond of shared values that stretches from Babylonian astronomy, through Greek atronomy, to Newtonian astronomy and beyond.

45. Kuhn, 1970: 94.
46. Kuhn, 1970: 10.
47. Dreyer, 1953: 345–346.
48. Neugebauer, 1968: 103.
49. Kuhn, 1957: 228.
50. Kuhn, 1957: 228.
51. Kuhn, 1962: 66.
52. Kuhn, 1962: 69.
53. Kuhn, 1957: 141.
54. Kuhn, 1962: 67.
55. Hall, 1954: 16.
56. Hall, 1957: 17.
57. Gingerich, 1975: 86.
58. Kuhn, 1962: 156.
59. Gingerich, 1975: 89.
60. Kuhn, 1957: 140.

61. Kuhn, 1962: 69.
62. Gingerich, 1975: 89.
63. Gingerich, 1975: 89–90.
64. Koyré, 1973: 26.
65. Swerdlow, 1973: 434.
66. Kuhn, 1957: 137.
67. Kuhn, 1967: 135.
68. Koestler, 1952: 332.
69. Brackenridge, 1982: 293. Put simply, the argument is that Kepler found that the orbital circle had to give way to the orbital ellipse in order to preserve the more fundamental celestial circularity of musical harmony, which was derived from the geometry of circles and expressed in the ratio of planetary angular velocities at aphelion and perihelion.
70. In *SSR*, Kuhn states, "Copernicanism made few converts for almost a century after Copernicus' death. Newton's work was not generally accepted, particularly on the Continent, for more than half a century after the *Principia* appeared." (Kuhn, 1970: 150) But one must make a clear distinction between the reception of Newton's work on the Continent and its reception in England. Clearly there are chauvinistic forces at work in France relative to the work of Descartes. In England, despite some concern over the "occult" nature of gravitational forces, there is a group of adherents that begins to form around the *Principia* almost at once.
71. Kuhn, 1978.
72. Most reviewers of Kuhn's 1978 work on quantum theory (note 56) indicated that they had expected such an analysis. In an essay review entitled "Paradigm Lost?", the writer states the common response: "The emergence of quantum theory at the beginning of this century heralded one of the most far-reaching scientific revolutions. Yet in Kuhn's current book, where he traces the early development of the quantum theory, few, if any, of his more general ideas on the nature of revolutions are evident." (Pinch, 1979: 437.)
73. Kuhn is not the only contemporary philosopher of science to be subjected to this criticism. In a recent work, David Stove argues that, in addition to Kuhn, the philosophers Popper, Lakatos, and Feyerabend all are irrationalists. (Stove, 1982, 3.)

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APPENDIX

Chronological Listing of Reviews

KUHN, THOMAS S. 1962.
The Structure of Scientific Revolutions
(Chicago).

GILLISPIE, CHARLES. 1962. *Science* 132: 1251–1253.

BARBER, B. 1963. *American Sociological Review* 28: 298–299.

BORING, E. G. 1963. *Contemporary Psychology* 8: 180–182.

HALL, M. D. 1963. *American Historical Review* 68: 700–701.

HAWKINS, D. 1963. *American Journal of Physics* 31: 554–555.

HESSE, M. 1963. *Isis* 54: 286–287.

SCHLEGEL, R. 1963. *Physics Today* 16: 69.

WILLIAMS, L. P. 1963. *Archives internationales d'histoire des sciences* 16: 182–184.

ARDLEY, G. 1964. *Philosophical Studies* 15: 183–192.

BOHM, D. 1964. *Philosophical Quarterly* 14: 377–379.

JORGENSEN, B. S. 1964. *Centaurus* 10: 48–50.

SHAPERE, D. 1964. *Philosophical Review* 73: 383–394.

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The second edition enlarged and
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BERRY, C. J. 1979. *British Journal for the History of Science* 12: 295–298.

HACKING, I. 1979. *History and Theory* 18: 223–236.

KOURANY, J. A. 1979. *Isis* 70: 279–280.

LUGG, A. 1979. *British Journal for the History of Science* 12: 289–295.

MULKAY, M. J. 1979. *British Journal for the History of Science* 12: 298–301.

SCHUSTER, J. A. 1979. *British Journal for the History of Science* 12: 301–314.

TOPPER, D. 1979. *Technology and Culture* 20: 218–220.

SIEGEL, H. 1980. *British Journal for the Philosophy of Science* 31: 359–384.

WILLIAMS, L. P. 1980. *History of Science* 18: 68–74.

Nuclear Power in the World Today*

MANSON BENEDICT

A reliable supply of electricity is essential to industrial society. Today, the principal means for generating electricity should be nuclear energy or coal. The best hydroelectric sites are fully utilized. Oil has become too expensive. Natural gas is a premium fuel which should be reserved for space heating and petrochemical production. Compared with coal, a nuclear plant has the advantages listed in figure 1 of being less vulnerable to interruptions in fuel supply by rail or mine strikes, or causing fewer injuries or deaths among workers or the general public, and of generating electricity at lower cost, except in a plant located right at a coal mine.

The second figure compares the cost of electricity in large base-load nuclear plants with the cost in large coal-fired plants using data on the Commonwealth Edison Co. in Illinois. The cost from these nuclear plants operating today is only about 60 percent of that of electricity from coal. The relative cost advantage projected for nuclear plants to be built in the next ten years is almost as great.

This paper describes briefly how a nuclear plant works, lists the amount of nuclear generating capacity now operating and planned in the principal industrial nations, and shows pictures of nuclear plants in a number of countries. It also describes the nuclear fuel cycle, the steps used in preparing fuel for nuclear power plants and reclaiming and disposing of spent fuel from them. I will close with some recommendations for the U.S. power program.

Figure 3 is a schematic diagram of a pressurized water nuclear power plant, the type used in about two-thirds of U.S. plants. Fission of uranium-235 in the core of the reactor heats pressurized primary water in the pressure vessel to about 300°C. This converts secondary water in the steam generator to steam, which drives a turbine which generates electricity.

The pressurized water in U.S. plants is natural water, for which uranium fuel must be enriched to contain about 3 percent of fissionable uranium-235. In Canadian plants, the primary water is heavy water, with which natural uranium containing only 0.7 percent uranium-235 can be used without enrichment.

Figure 4 is a schematic diagram for a boiling water nuclear power plant used in about one-third of U.S. plants. It differs from the pressurized water types in that natural water is allowed to boil in the reactor core, and the steam thus produced drives the turbine directly.

Both the pressurized water and boiling water reactors produce some fissionable plutonium from the uranium-238 in their fuel, but not enough to compensate for the fissionable uranium-235 consumed. By using a liquid metal, sodium, to transport heat from the reactor instead of water, fission takes place with fast neutrons, and plutonium production is so increased that the reactor can produce more fissionable material than it consumes and is said to "breed." Figure 5 is a diagram of a sodium-cooled, liquid-metal fast breeder reactor. Large breeder reactors are operating in England, France and the Soviet Union. The Reagan administration is ex-

Advantages of Nuclear Energy Over Coal for Generating Electricity
1. More secure fuel supply
2. Fewer injuries or deaths to workers and public
3. Lower cost

FIG. 1. Advantages of Nuclear Power

Cost of Electricity from Large, Base Load Stations Commonwealth Edison Company

	Cents per kilowatt-hour	
	Nuclear	Coal
Actual, present stations	1.7	3.0
Projected, stations operational in 1991*	13.3	18.2

G. R. Corey, to be published in *Annual Review of Energy*, 1981
* Assuming 7.5% annual cost escalation

FIG. 2. Cost of Electricity

Pressurized water reactor (PWR)
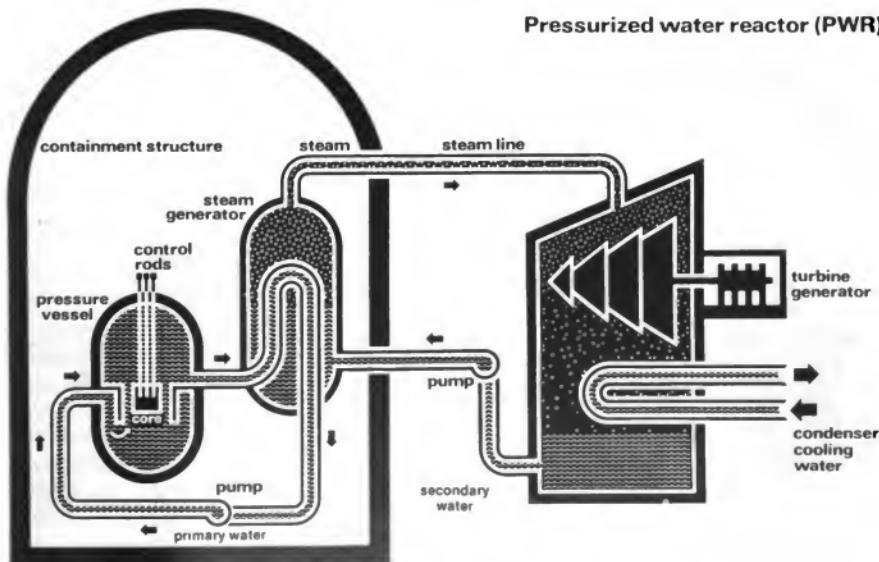
FIG. 3. Pressurized Water Reactor

Boiling water reactor (BWR)
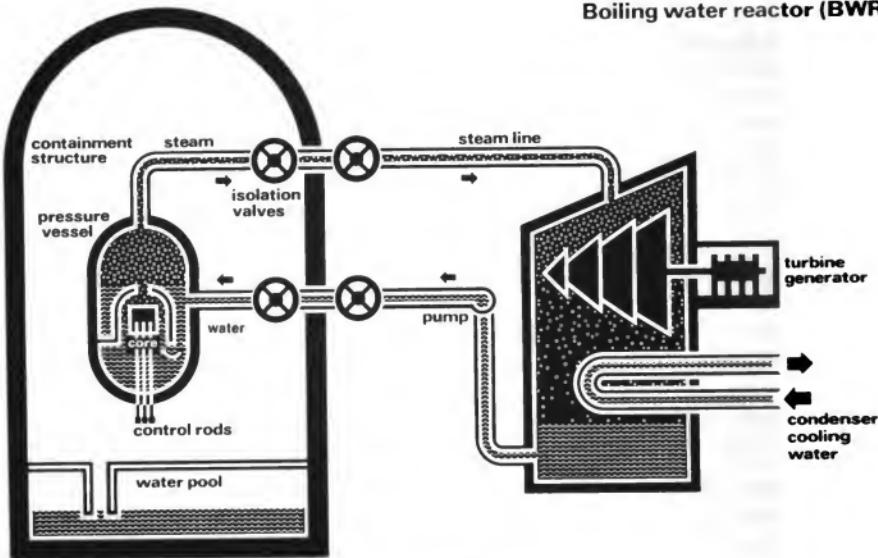
Fig. 4. Boiling Water Reactor

Liquid metal fast breeder reactor (LMFBR)
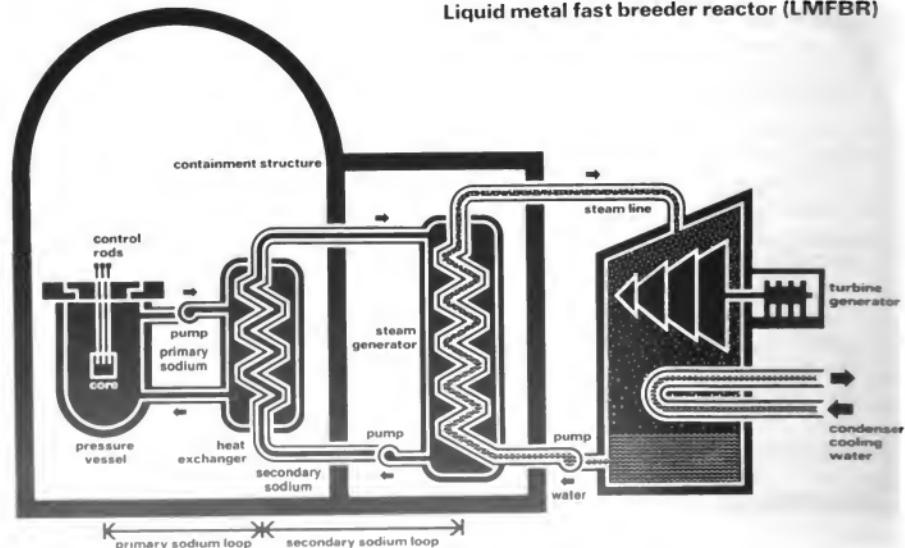
Fig. 5. Liquid Metal Fast Breeder Reactor

pected to complete construction of the similar Clinch River Breeder Reactor, which was stopped by the Carter Administration. The big advantage of the breeder reactor is that it makes available as nuclear fuel the 99.3 percent of natural uranium which is non-fissionable uranium-238.

Figure 6 is a map showing the location of nuclear power plants in the United States. Plants now operating are marked by black circles; others under construction or on order, by open symbols. Figure 7 is a photograph of the Donald C. Cook pressurized water plant on Lake Michigan; figure 8 is the Pilgrim Boiling Water Station on Massachusetts Bay.

The next two figures show Canadian nuclear facilities: the four Pickering Heavy-Water Nuclear Power Plants of Ontario Hydro, near Toronto and that company's Bruce Nuclear Power Station on Lake Huron, with a heavy water production plant in the foreground with its tall fractioning towers.

Figure 11 gives the total nuclear generating capacity of countries in North and South America at present and as projected. By 1990 about 15 percent of their electric capacity is expected to be nuclear.

Figure 12 is a similar table for western Europe. France leads in planned use of nuclear energy, with 65 percent of its electric capacity expected to be nuclear by 1990. Breeders are planned in France, England and West Germany. Gas-cooled reactors are used in England; the Magnox type at Oldbury is shown in figure 13; the advanced gas-cooled type at Hinckley Point in figure 14. Figure 15 shows the big French nuclear complex at Ticastin, with four pressurized water reactors in the foreground and the large Eurodif gaseous diffusion plant to enrich uranium in the background. Figure 16 shows the 250-megawatt French breeder reactor Phenix which has been operating successfully since 1974, and figure 17 shows the 1200-megawatt Super-Phenix reactor scheduled to operate in 1983.

The nuclear-generating capacity of Soviet-block nations, with the Soviet Union having most of the capacity is listed in figure 18. Breeders, light-water reactors and graphite-moderated reactors are in operation there.

Figure 19 lists the nuclear generating capacity of Asian nations. Japan is the leading nation, using mostly light water reactors, but with one small breeder reactor and a heavy water reactor. Figure 20 shows the Mihama pressurized water power plant and figure 21 the Fugen heavy water station.

Nuclear power plants differ from coal-fired plants in requiring novel facilities to produce fuel for them and process fuel from them. Figure 22 shows the principal steps in the nuclear fuel processing plants making up what is called the nuclear fuel cycle.

The first step is mining uranium ore, which contains only a few pounds of uranium per ton. Uranium in the ore is concentrated in a uranium mill located near the mine. Uranium concentrates are shipped to a uranium refinery where impurities are removed and the uranium is converted to the chemical form needed in the next step, uranium hexafluoride in this slide. This is the only stable, volatile compound of uranium. It is needed as feed for plants to enrich the fissionable isotope uranium-235, using the gaseous diffusion or gas centrifuge process. Enriched hexafluoride from such plants is converted to uranium dioxide. This ceramic material is formed into pellets and fabricated into reactor fuel elements in a fuel element factory.

After use in the nuclear power plant, spent fuel is very radioactive but contains enough residual uranium-235 and plutonium to warrant their recovery. This may be done in a reprocessing plant, where the fuel is dissolved in nitric acid and the uranium and plutonium are separated from radioactive fission products by extraction with an immiscible solvent. The uranium may be converted back to the hexafluoride and recycled to the enrichment plant. The plutonium may be used as startup feed for a breeder reactor.

Nuclear Power Plants in the United States

75	Reactors with operating licenses	55,791 MWe
82	Reactors with construction permits	90,503 MWe
2	Reactors with limited work authorizations	2,300 MWe
15	Reactors on order (including 2 units	17,542 MWe
	not sited on map)	
174	Total	166,136 MWe

December 31, 1980

FIG. 6. Nuclear Power Plants in the United States

Key

● Operable
○ Under Construction
□ With Limited Work Authorization
△ On Order
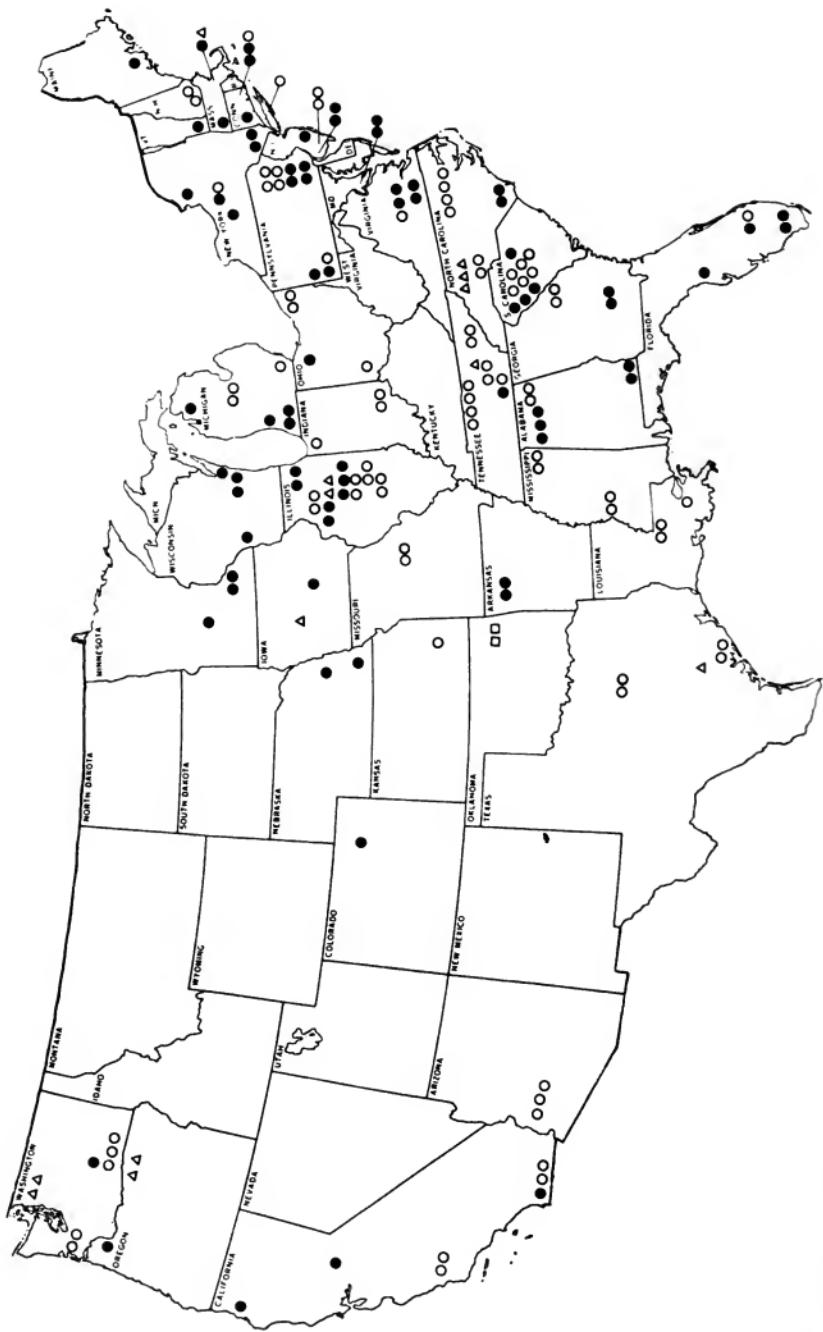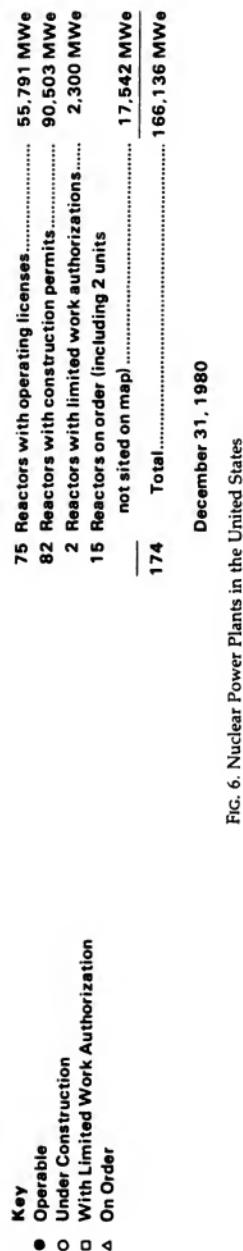
Fission products may be converted to a water-insoluble glass to be stored in an underground repository.

The amount of uranium mined per year and the total uranium resources of the principal uranium-producing nations are listed in figure 23. A typical 1000-megawatt light water reactor consumes about 140 metric tons of uranium per year. Present U.S. uranium production is sufficient to fuel about 100,000 megawatts of pressurized water nuclear power plants. The leading uranium-producing nations are the United States, with about 40 percent of the world's capacity, Canada with 18 percent and South Africa with 13 percent.

Separation of uranium-235 from uranium-238 is very difficult because these two isotopes have nearly identical properties. Figure 24 shows two of the large stages used in the U.S. Department of Energy's diffusion plants. The U.S. has three diffusion plants. When they were in full operation in the 1960s, they consumed five percent of all U.S. electricity.

The U.S. Department of Energy is developing a more energy-efficient process to separate uranium isotopes, the gas centrifuge, which works on the same principal as a cream separator. A similar centrifuge separation process is now being used by a consortium of British, Dutch and German companies called Urenco, whose pilot plant is at Almelo, Holland. The gas centrifuge uses much less energy than gaseous diffusion.

Reprocessing plants to separate uranium and plutonium from fission products in spent fuel discharged from nuclear power plants are in operation in England, France and Japan. The next three figures show reprocessing plants at Windscale, England, at La Hague, France, and at Tokai, Japan, which I visited in November 1980.

A private U.S. company built a reprocessing plant in Barnwell, South Carolina, but the Carter administration refused it permission to operate, in an unsuccessful attempt

FIG. 7. Donald C. Cook Nuclear Power Plant

FIG. 8. Pilgrim Nuclear Power Plant

FIG. 9. Pickering Nuclear Power Station

FIG. 10. Bruce Nuclear Complex

Nuclear Generating Capacity in Americas							
		Actual 1980		Projected 1985		Projected 1990	
	Type	MW	%	MW	%	MW	%
Argentina	H, L	344	3	944	8	1,642	12
Brazil	L	0		626		10,586	13
Canada	H	5,514	8	9,700	10	16,900	15
Chile	?	0		0		600	15
Cuba	L	0		880			
Mexico	L	0		1,308	5		
U.S.A.	L, B?	55,791	10	104,417	15	138,916	17

MW = Megawatts of nuclear electric generating capacity

% = Percent of national generating capacity which is nuclear

H = Heavy water   L = Light water   B = Breeder

FIG. 11. Nuclear Generating Capacity in Americas

Nuclear Generating Capacity in Western Europe							
		Actual 1980		Projected 1985		Projected 1990	
	Type	MW	%	MW	%	MW	%
Belgium	L	1,667	16	5,427	38	12,200	
Finland	L	1,080	10	2,160	20	5,000	30
France	B, G, L	8,330	10	33,125	50	50,000	65
Italy	G, L	1,412	3	2,434	5	13,400	15
Netherlands	L	505	3	505	3	505	3
Spain	L	1,082	4				
Sweden	L	3,700	15	8,380	28	9,430	
Switzerland	L	1,926	18	2,871	22		
United Kingdom	B, G, L	6,426	10	10,196	11	12,836	13
West Germany	B, L	8,887	12	19,534		26,580	

MW = Megawatts of nuclear electric generating capacity

% = Percent of national generating capacity which is nuclear

G = Gas-cooled   B = Breeder   L = Light water

FIG. 12. Nuclear Generating Capacity in Western Europe

FIG. 13. Oldbury Magnox Nuclear Power Station

to persuade other nations not to recover plutonium. I hope that the Reagan administration will permit this plant to operate, under proper safeguards to prevent misuse of plutonium, so that the uranium and plutonium in spent fuel can be used to augment U.S. nuclear fuel supplies.

Reprocessing plants produce highly radioactive waste in the form of a water solution. Before such waste can be stored

FIG. 14. Hinckley Point B AGR Nuclear Power Station

Fig. 15. Nuclear Complex, Tricastin, France
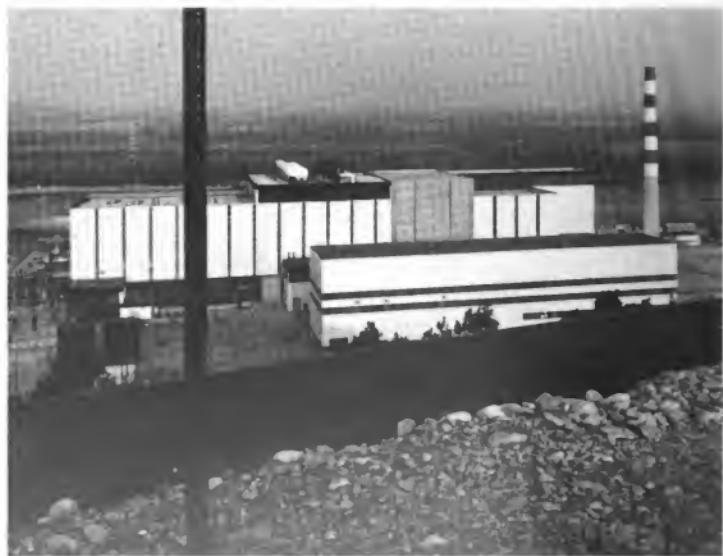
Fig. 16. French Fast Breeder Reactor Phenix
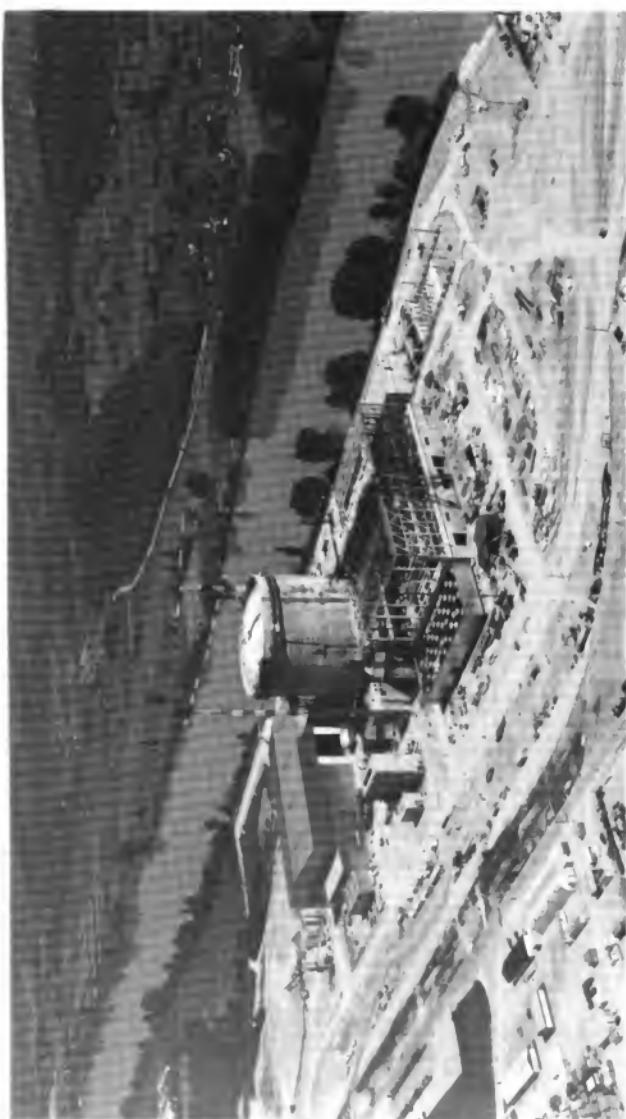
Fig. 17. French Fast Breeder Reactor Superphenix

Nuclear Generating Capacity in Soviet Bloc							
		Actual 1980		Projected 1985		Projected 1990	
	Type	MW	%	MW	%	MW	%
Bulgaria	L	880		1,760		5,760	35
Czechoslovakia	L	112		4,952	17		32
East Germany	L	1,400		5,360			
Hungary	L	0		1,760		4,760	10
Poland	L	0		440		4,880	9
Romania	L	0		440			20
Soviet Union	B, C, L	9,905	4	34,135	10		25

MW = Megawatts of nuclear electric generating capacity

% = Percent of national generating capacity which is nuclear

L = Light water reactor   B = Breeder

C = Graphite moderated, water cooled reactor

FIG. 18. Nuclear Generating Capacity in Soviet Bloc

Nuclear Generating Capacity in Asia							
		Actual 1980		Projected 1985		Projected 1990	
	Type	MW	%	MW	%	MW	%
India	L, H	596	2	1,676	4	2,116	5
Indonesia	?	0		1,600		2,900	
Japan	L, H, B	14,952	12	30,000	17	53,000	25
Pakistan	H, L	125		725			
Phillipines	L	0		620	10	620	7
South Korea	L, H	587	8	3,815	20		
Taiwan	L	1,212	17	4,928	31		
Thailand	?	0		0		900	10

MW = Megawatts or nuclear electric generating capacity

% = Percent of national generating capacity which is nuclear

L = Light water   H = Heavy water   B = Breeder

FIG. 19. Nuclear Generating Capacity in Asia

Fig. 20. Mihama-1 Nuclear Power Station

Fig. 21. Fugen Heavy Water Reactor
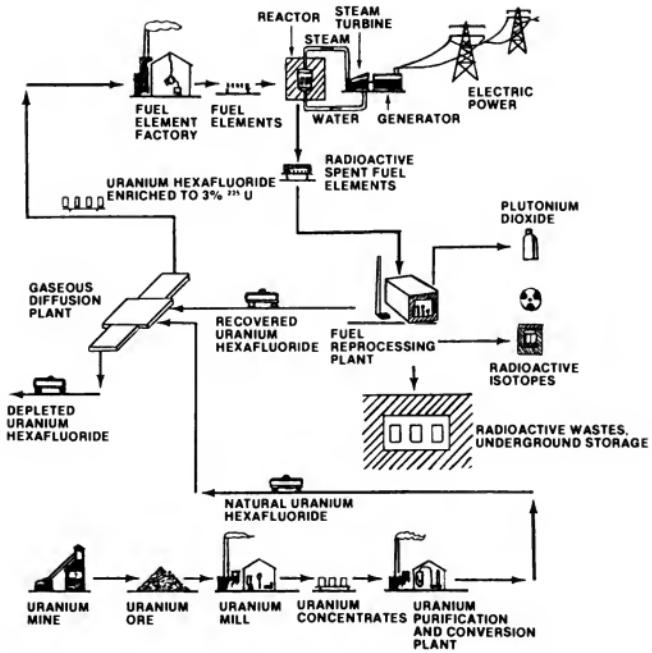
FUEL-CYCLE OPERATIONS FOR LIGHT-WATER REACTOR

Fig. 22. Fuel Cycle Operations for Light Water Reactor

without constant monitoring it must be converted into a water-insoluble solid. Processes for evaporating this water solution to dryness and converting it into a water-insoluble glass have been perfected in the United States, England, France, Germany and Japan, and are being operated on an industrial scale in France. Glass is stable in the presence of radioactivity; it resists leaching by underground waters; it accommodates a variety of waste compositions; and it can be readily produced from radioactive materials. Finally, the glass is packaged in hermetically sealed, corrosion-resistant metal cans.

The last step in the nuclear fuel cycle is safe storage of nuclear wastes. At present in the United States unreprocessed spent fuel elements are being stored in water-cooled basins at nuclear power plants and at inactive reprocessing plants. In France glassified waste is being stored in air-cooled concrete vaults. Such storage is safe, but it is unsatisfactory as a permanent measure because it requires continuous guarding to prevent human intrusion.

The procedure presently favored for permanent, untended storage of highly radioactive waste is burial in geologic strata deep underground where circulating grounds waters are demonstrably absent. Suitable geologic formations are monolithic granite, such as underlies much of Sweden; basalt, found in the United States; and salt deposits, such as occur in Germany and many states of our

National Uranium Production Rates and Resources (Exclusive of Soviet Bloc)		
	1979 Uranium production rate, metric tons per year	Uranium resources, thousand metric tons
Australia	600	352
Brazil	103	164
Canada	6,900	963
France	2,180	101
Gabon	1,000	37
India	0	54
Namibia	3,692	186
Niger	3,300	213
South Africa	5,195	530
Sweden	0	304
United States	14,800	1,866
Others	609	273
Total	38,379	5,043

Source: OECD nuclear energy agency and international atomic energy agency: "Uranium—resources, production and demand," December 1979

Fig. 23. National Uranium Production Rates and Resources

Fig. 24. Gaseous Diffusion Equipment
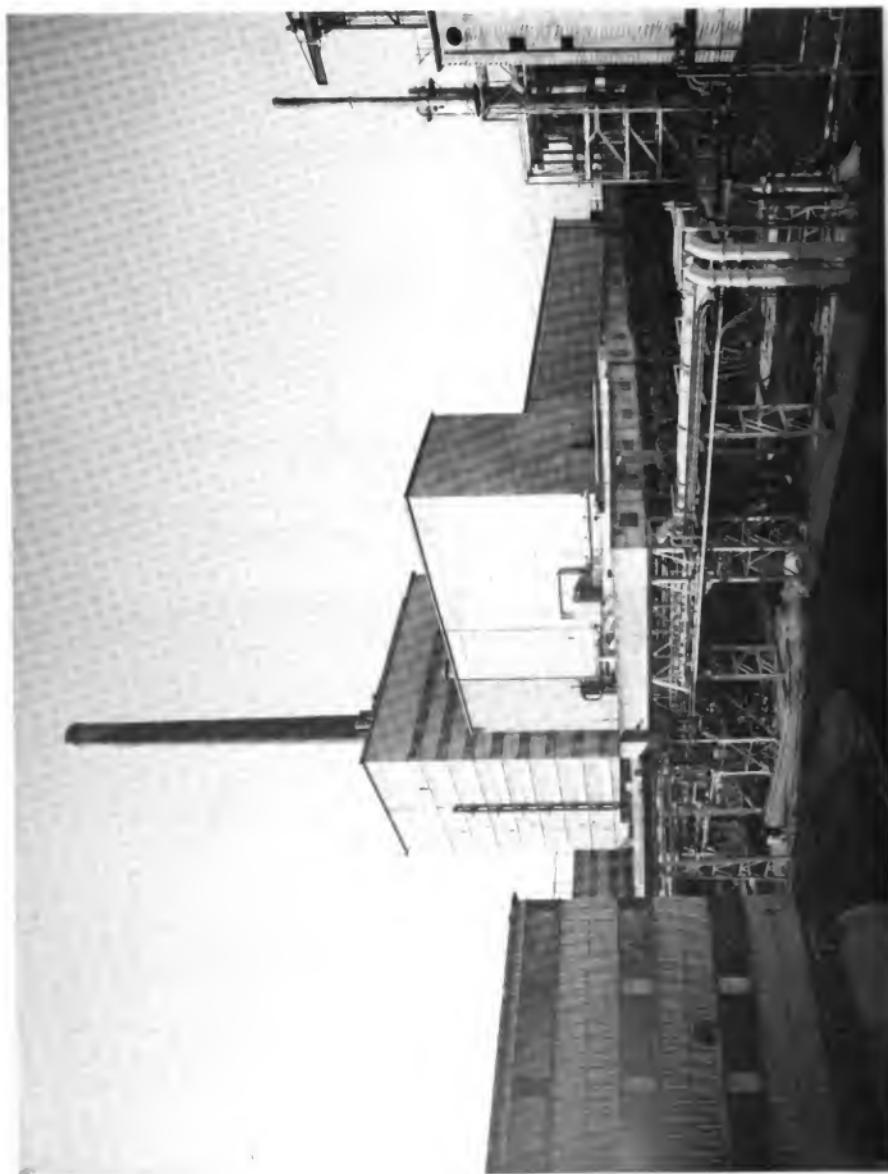
Fig. 25 Windscale Reprocessing Plant

FIG. 26. La Hague Reprocessing Plant

FIG. 27. Tokai Reprocessing Plant

own country. A committee of the U.S. National Academy of Sciences of which I was a member concluded that wastes could be stored safely in this manner and recommended construction of a pilot waste repository in a New Mexico salt deposit. This program has been delayed by political difficulties; no one state is eager to accept radioactive wastes from other states. In Germany, despite similar public relations problems, work is proceeding on a pilot waste repository in a mined out salt deposit at Asse, shown in figure 28. I can't emphasize too strongly the necessity of processing in the United States with demonstration that nuclear wastes can be stored safely in such an underground repository. This is one of the most critical factors impeding public acceptance of nuclear power.

I conclude this brief world tour of nuclear power facilities by summarizing my recommendations for the United States:

First, we should substitute electricity, nuclear or coal-generated, for oil or gas wherever possible.

Second, we should facilitate construction of the present generation of water-cooled nuclear power plants by providing better public understanding of their economy and safety and by reducing delays in building and licensing them.

Third, we should expedite development of the breeder to ensure long-term availability of nuclear energy.

Fourth, we should complete construction and operation of the Barnwell, South Carolina reprocessing plant.

Fifth, we should commission an under-

FIG. 28. Radioactive Waste Storage at Salt Mine, Asse, West Germany

ground federal pilot repository for radioactive wastes.

If the Reagan administration will take these five steps, nuclear energy will become a major factor in maintaining the quality of life in the United States.

RECOMMENDATIONS

1. Substitute Electricity, Nuclear or Coal-Generated for Oil and Gas.
2. Facilitate Construction of Conventional Nuclear Plants.
3. Expedite Development of the Breeder.
4. Complete Construction and Start Operation of Barnwell Reprocessing Plant.
5. Commission an Underground Repository for Radioactive Wastes.

FIG. 29. Recommendations

PROCEEDINGS

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VOLUME 129

1985

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